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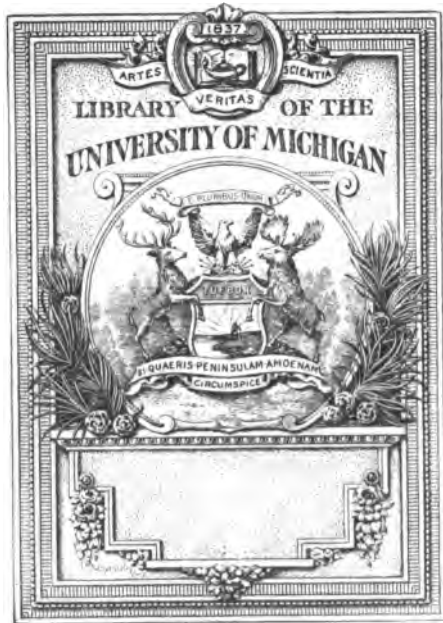
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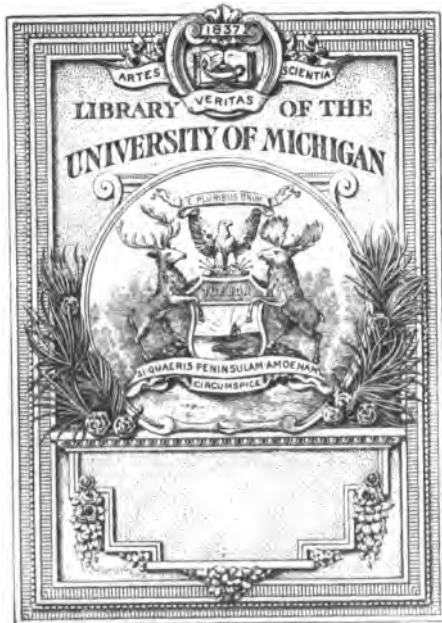
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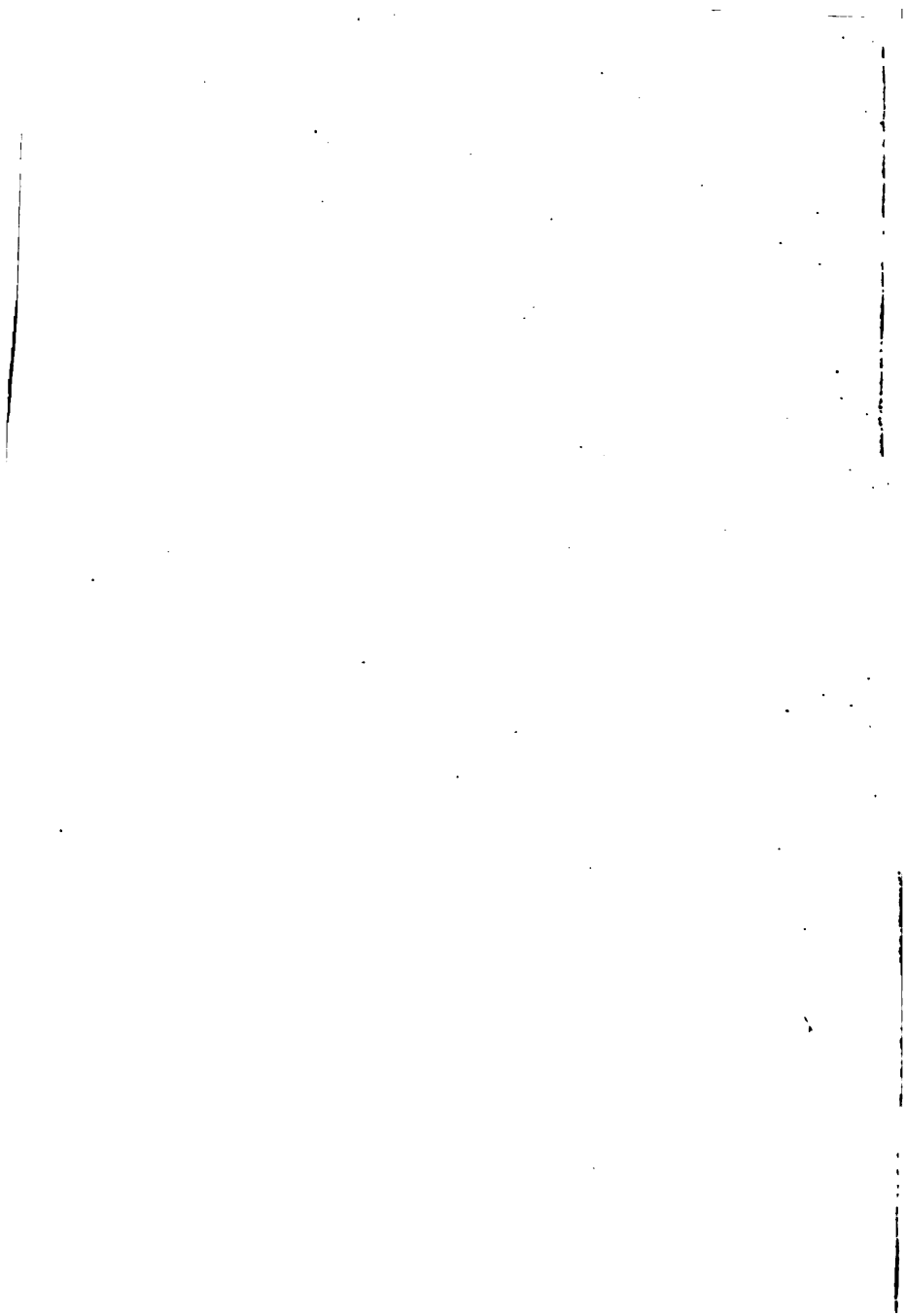
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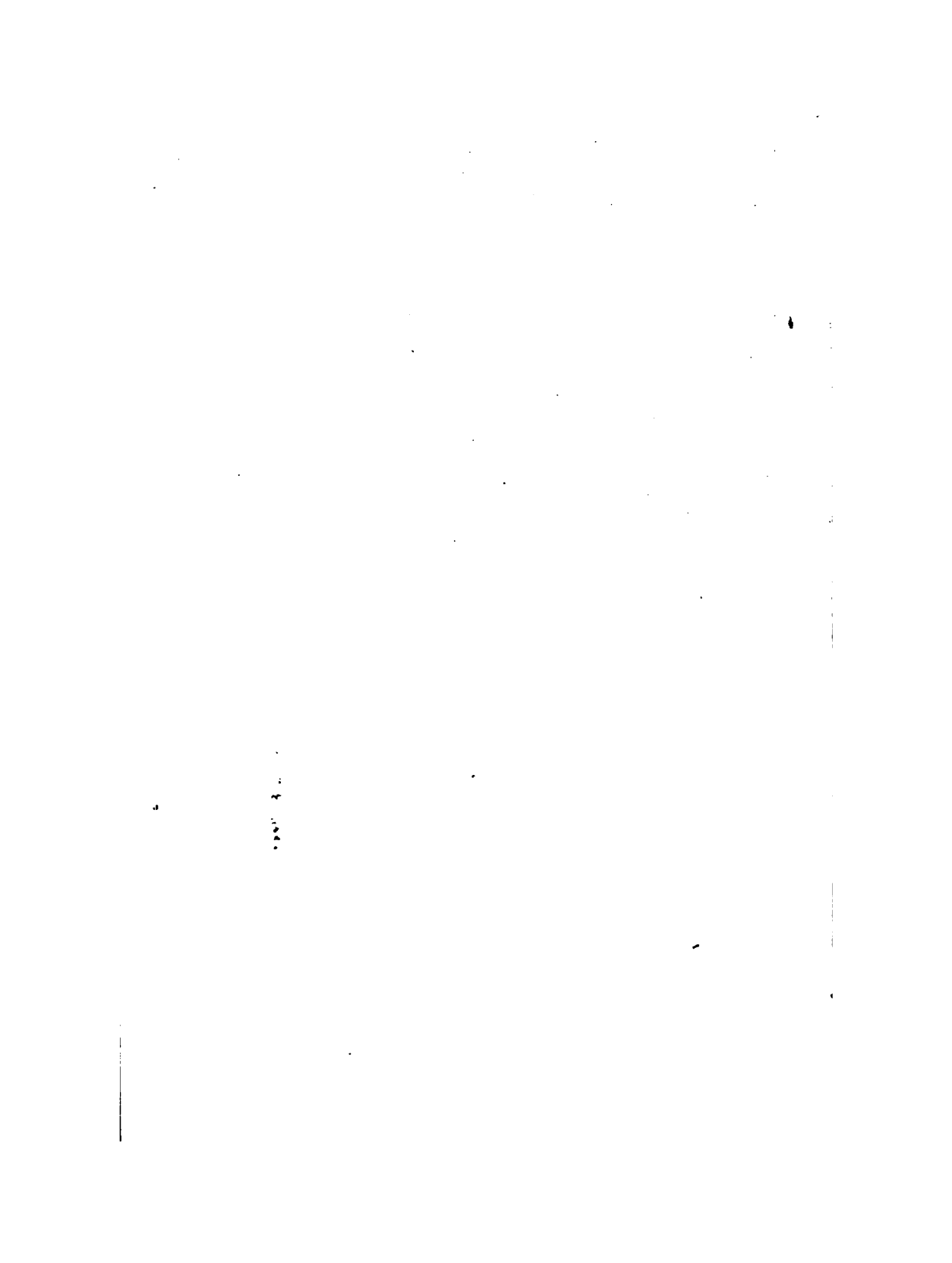
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**PHYSICAL CHEMISTRY**





# PHYSICAL CHEMISTRY

FOR

PHYSICIANS AND BIOLOGISTS

BY  
*Julius*

DR. ERNST COHEN

*Professor of General and Inorganic Chemistry in the  
University of Utrecht*

*AUTHORIZED TRANSLATION FROM THE GERMAN*

BY

MARTIN H. FISCHER, M.D.

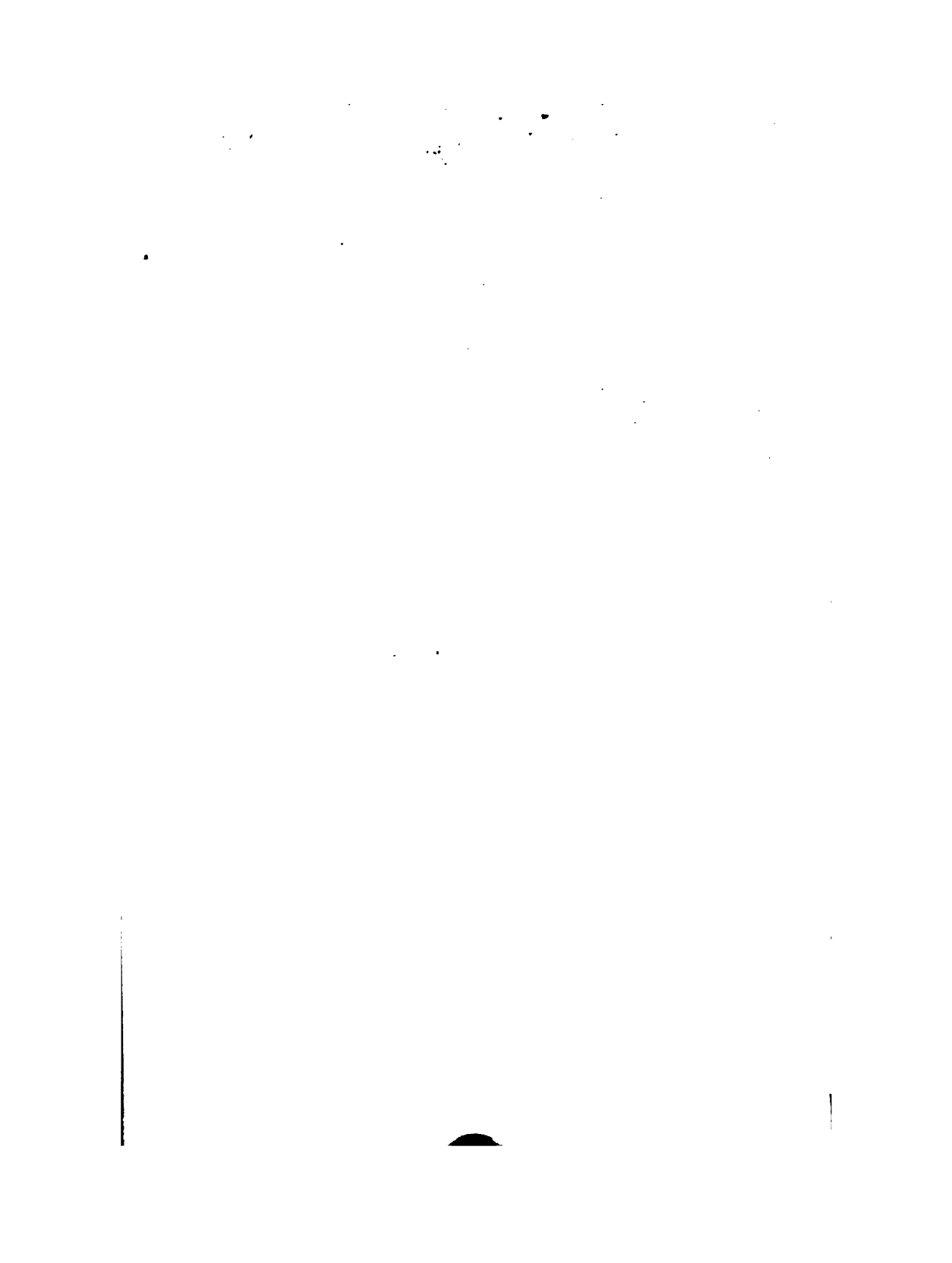
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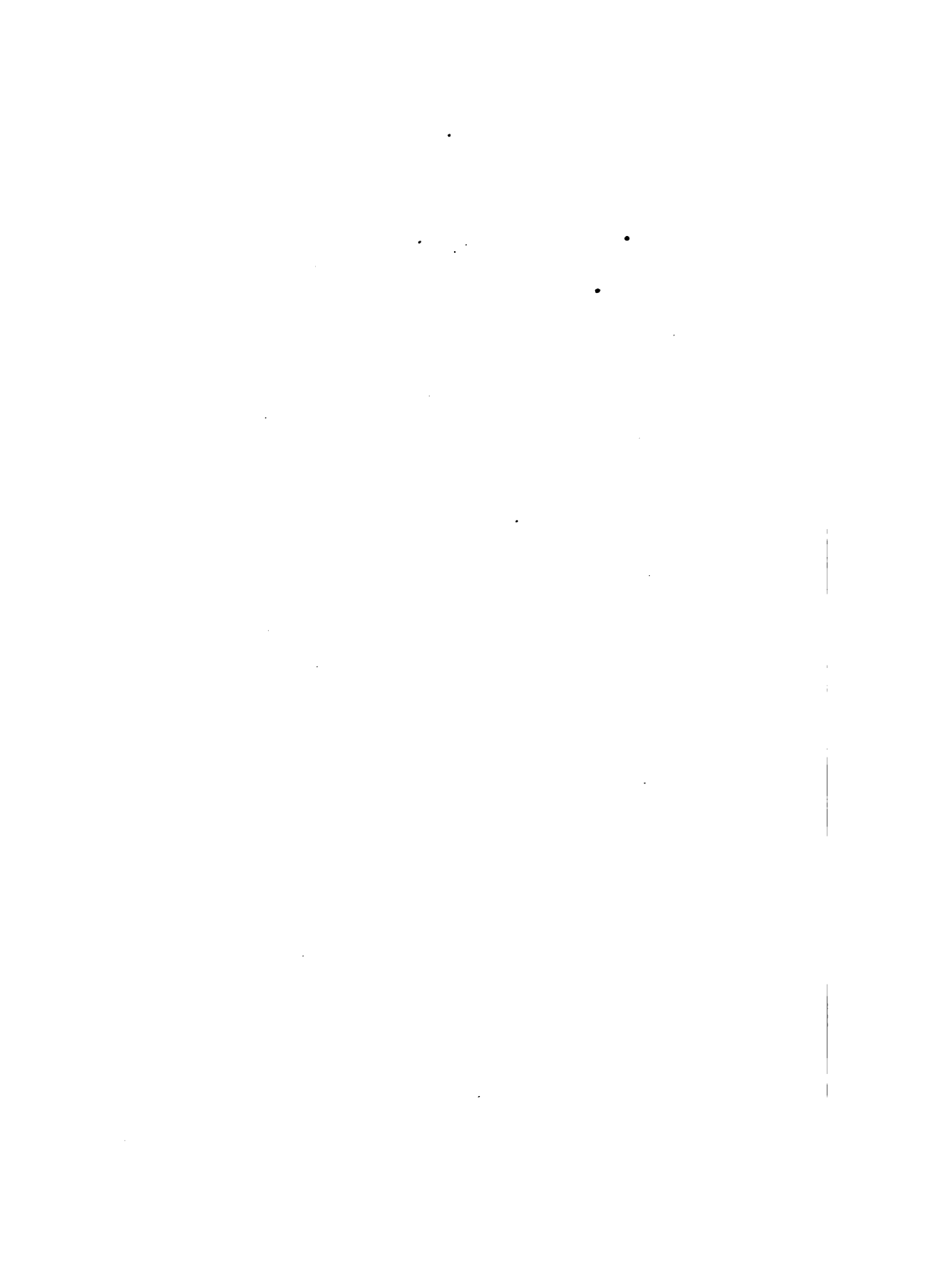
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To  
**PROF. DR. HECTOR TREUB.**



## NOTE TO THE AMERICAN TRANSLATION.

THE development of physiology and biology has, during the last years, been so decidedly under the influence of physical chemistry, that those who wish to follow the progress of the former science must be familiar with the principles of the latter. Prof. Cohen's book not only serves as an introduction to physical chemistry, but also teaches the physician and the biologist how to apply this science to medical and biological problems. This combination gives it a unique place in the literature of physical chemistry, and for this reason, as well as for the masterly treatment of the subject, I encouraged Dr. Fischer to undertake, with the consent of Prof. Cohen, an English translation of his book.

JACQUES LOEB.

UNIVERSITY OF CALIFORNIA.

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## TRANSLATOR'S PREFACE.

THAT accuracy of expression which is so obvious a characteristic of Prof. Cohen's book the translator has endeavoured to preserve, perhaps at the partial sacrifice sometimes of English idiom.

The translation has had the benefit of a revision by Prof. Cohen, who has made numerous corrections and additions. I also acknowledge with much pleasure my indebtedness to Dr. Herbert N. McCoy of the University of Chicago, whose careful criticisms and suggestions have much improved the quality of the translation.

MARTIN H. FISCHER.

BERKELEY, CALIFORNIA,  
November 29, 1902.

## AUTHOR'S PREFACE.

I HAVE prepared the following pages in response to the request of a number of physicians to give in a series of lectures a résumé of those subjects in physical or general chemistry which are of importance in medicine.

The fact that a large number of observations are described in modern medical literature that are based upon our newer conceptions of physical chemistry renders it imperative that the physician become acquainted with these theories and methods if he does not wish to have such observations and their practical applications remain a sealed book to him.

These lectures are in no way a text-book of physical chemistry. I have merely endeavoured to show in them the close relation that exists between this new branch of chemistry and the biological sciences, and also, in response to the wishes of my hearers, to describe in some detail the more important methods of physical chemistry.

The book may perhaps serve as an introduction to the study of the excellent text-books now available devoted to physical chemistry.

Should the lectures contained in the following pages incite any one to a study of this subject and to its application to the medical sciences, the purpose of this volume will have been accomplished.



*AUTHOR'S PREFACE*

In conclusion I wish to express my thanks to my friend Professor Georg Bredig, who very kindly assisted me in correcting the proofs, and to Dr. J. M. Baart de la Faille for many helpful suggestions.

ERNST COHEN.

AMSTERDAM, August 1901.

## INTRODUCTION.

I CONSIDER it a happy sign of the times that such a group of medical men as you have evinced the desire to study more closely the acquisitions of *general* or *physical* chemistry within the last fifteen years.

That the views and methods to which this young branch of our scientific knowledge has led can be of the greatest value to the physician is evidenced in a most striking way by the fact that these find daily a more far-reaching application to the problems of physiology, pharmacodynamics, and biology.

May my lectures assist in convincing you of the great value that the study of this beautiful science has for the physician!

So far as the subject-matter that is here to be discussed is concerned, I believe that, in view of the limited number of lectures, any definite system may be relegated to the background. The chapters about to be discussed will deal as far as possible with those problems which are of greatest interest to the medical man who devotes himself to experimental research; while at the same time his attention will be directed to the results that have already been obtained in this direction.



## FIRST LECTURE.

### Reaction Velocity.

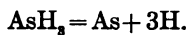
WE take as our starting-point the *law of chemical mass action* (Guldberg and Waage, 1867), which states that in chemical reactions the chemical action is proportional to the *active mass* of the reacting substances; the *active mass* of a substance is the amount of the same in the unit of volume (*concentration*).

If a number of substances capable of reacting chemically with each other are brought together, a reaction ensues which after a certain time comes (practically) to a standstill; we say then that the system is in *equilibrium*. Both the course of the reaction and the equilibrium which is established at the end of the reaction are governed by the law of Guldberg and Waage.

If we consider the simplest case, one in which only one molecule of a substance undergoes decomposition, we deal with a

#### A. MONOMOLECULAR REACTION

If, for example, hydrogen arsenide is heated in a glass tube, the gas is split into arsenic and hydrogen, according to the equation



We call this decomposition a monomolecular one, since the reaction occurs in the simple molecule  $\text{AsH}_3$ .

Since, however, the arseniuretted hydrogen disappears during the reaction (being decomposed into its constituents by heating) according to the law of Guldberg and Waage, the velocity of decomposition cannot remain constant; the decomposition velocity must progressively decrease, since the active mass of hydrogen arsenide progressively decreases. If we imagine that during each minute a tenth of the arseniuretted hydrogen present at the time is decomposed, we get after 1, 2, 3, etc., minutes the following degrees of decomposition:

Time.	Amount of Substance Present.	Amount Decomposed (per Minute).
0-1	1.000	$0.1 \times 1.000 = 0.100$
1-2	$(1.000 - 0.100) = 0.900$	$0.1 \times 0.900 = 0.0900$
2-3	$(0.900 - 0.0900) = 0.810$	$0.1 \times 0.81 = 0.0810$
3-4	$(0.810 - 0.081) = 0.729$	$0.1 \times 0.729 = 0.0729$
4-5	$(0.729 - 0.0729) = 0.656$	$0.1 \times 0.656 = 0.0656$
etc.	etc.	etc.

At the beginning of the reaction the amount 1.000 was present. According to our assumption, one tenth of this (0.1) is decomposed per minute, so that at the end of the first minute the amount of undecomposed substance still present is  $1.000 - 0.1 \times 1.000 = 0.900$ . Of this amount a tenth part is decomposed in the second minute, that is to say,  $0.1 \times 0.900 = 0.0900$ ; at the end of the second minute the amount of substance still undecomposed is therefore  $0.900 - 0.0900 = 0.810$ ; and so on. If  $C$  is the concentration of the hydrogen arsenide at the time  $t$  [ $C$  is measured in gram-molecules\* per litre, that is to say, we call

\* Instead of the word *gram-molecule*, at Ostwald's suggestion the shorter term *mol* is often used.

the concentration of the arseniuretted hydrogen 1 when each litre contains 1 mol (=78 g. hydrogen arsenide, since As=75, H<sub>3</sub>=3)] and  $dC$  is the slight change that the concentration of the solution suffers in a very short time  $dt$ , then we can express the law, the reaction velocity is proportional to the concentration, as follows:

$$-\frac{dC}{dt} = kC. \quad (1)$$

$\frac{dC}{dt}$  is the reaction velocity, that is, the relation between the quantity decomposed and the time required for this decomposition;  $\frac{dC}{dt}$  has a minus sign before it because the concentration of the arseniuretted hydrogen decreases as the time increases, that is, as the value of  $t$  becomes greater.

The significance of the factor  $k$  is found immediately when we substitute in the above "differential equation"  $C=1$ ;  $k$  is the reaction velocity when the substance undergoing decomposition has the unit of concentration.  $k$  is called the *velocity constant* or the *reaction constant*. The above equation therefore shows us in what way the very slight (infinitely slight) change in the concentration ( $dC$ ) in a very short (infinitely short) period of time ( $dt$ ) is connected with the concentration ( $C$ ) of the substance undergoing decomposition.

But it is impossible to perform an experiment that will last only an infinitely short time. Every experiment occupies a definite time, and with nothing further the above equation would, for practical purposes, be useless. But integral calculus teaches us how the infinitely small changes in concentration ( $dC$ ) in the infinitely small periods

of time ( $dt$ ) may be summed up, and how from this the (finite) change in concentration in a certain limited time may be calculated.

Through "integration" the equation is rendered applicable to the experimental data.

This mathematical procedure, "integration," yields the result that between the concentration  $C$  and the time  $t$ , when the system has this concentration, the following relation always exists:

$$-l \cdot C = kt + \text{constant.} \quad (2)$$

In this equation  $l \cdot C$  represents the natural logarithm of the concentration. If the measured concentration of the substance undergoing decomposition is at the time  $t_1$  equal to  $C_1$ , at the time  $t_2$  equal to  $C_2$ , then, according to equation (2),

$$\begin{aligned} -l \cdot C_1 &= kt_1 + \text{constant} \\ -l \cdot C_2 &= kt_2 + \text{constant} \\ \hline -l \cdot C_2 + l \cdot C_1 &= k(t_2 - t_1) \\ l \cdot \frac{C_1}{C_2} &= k(t_2 - t_1) \\ k &= \frac{1}{t_2 - t_1} l \cdot \frac{C_1}{C_2}. \quad (3) \end{aligned}$$

In this equation we are dealing solely with values that are determined by experiment; we can therefore calculate  $k$ .

In this way, for example, the value of  $k$  for arseniuretted hydrogen at  $302^\circ$  C. was found to be

$$k = 0.0175.$$

What now does this figure signify chemically considered?

It shows that the decomposition velocity of hydrogen arsenide at  $302^\circ$  is such that, if during the unit of time the amount of arseniuretted hydrogen that undergoes decomposition is kept constant through the replacement of the decomposed part by an equal amount of new material, at the end of this time 0.0175, or 1.75 per cent, of the amount

originally present has been decomposed. It is assumed that the products of the reaction, in this case arsenic and hydrogen, are removed as soon as formed.

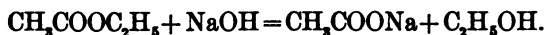
In the literature we often find equation (3) stated in a somewhat different form. If the concentration of the substance undergoing decomposition is equal to  $A$  at the beginning of the experiment ( $t = 0$ ), and if the amount decomposed at the time  $t$  is  $x_1$ , then the concentration of the undecomposed substance at this time is  $A - x_1$ , and this value is equal to  $C_1$  in the equation (3). If the amount decomposed at the time  $t_2$  equals  $x_2$ , then  $A - x_2$  can be substituted for  $C_2$ . Equation (3) then assumes the following form:

$$k = \frac{1}{t_2 - t_1} l \cdot \frac{A - x_1}{A - x_2}.$$

The gradual decomposition of the hydrogen arsenide indicates that all the molecules of a gas do not exist in the same state; if they did, then the decomposition of all the molecules would occur simultaneously or not at all.

#### B. BIMOLECULAR REACTION.

A chemical reaction in which two molecules react with each other we call a bimolecular reaction. We choose as an example a reaction that has been of excellent service in the study of many weighty problems in physical chemistry,—the saponification of esters by bases. If we take the case in which ethyl acetate is saponified by sodium hydroxide, we can represent the reaction by the following equation:



If dilute aqueous solutions of ethyl acetate and sodium hydrate are mixed together, double decomposition can occur between the two dissolved substances only where



their molecules come in contact with each other. The number of such collisions, it is evident, will be proportional to the number of ethyl acetate molecules present in the unit volume of solution. The same may be said regarding the sodium hydroxide molecules.

If, now, the concentration of the ethyl acetate is  $C_1$ , that is, if in each litre there are present  $C_1$  mols  $\text{CH}_3\text{COOC}_2\text{H}_5$ , and if the concentration of the sodium hydroxide is  $C_2$ , that is,  $C_2$  mols NaOH per litre, then

$$-\frac{dC_1}{dt} = k_1 C_1 C_2 \quad \text{and} \quad -\frac{dC_2}{dt} = k_1 C_1 C_2.$$

These two differential equations, from which are determined the course of the bimolecular reaction, may be reduced to one, if we assume that the ethyl acetate and the sodium hydroxide are present in equivalent amounts in the solution, that is to say, in such proportions that during each moment of time the two substances unite perfectly with each other.

If the concentration of the ethyl acetate is represented by  $C$ , then, under the assumed conditions of the equivalence of the substances present, the concentration of the sodium hydroxide is also  $C$ , and the equation governing the course of the reaction is

$$-\frac{dC}{dt} = kC \times C = kC^2.$$

Integration of this equation gives

$$\frac{1}{C} = kt + \text{constant.} \quad (1)$$

How now can we determine the value of  $k$  experimentally?

To do this we ascertain the concentration,  $C_1$ , of the sodium hydroxide (or of the ethyl acetate) at the time  $t_1$ , and the concen-

tration  $C_1$  of the sodium hydroxide (or of the ethyl acetate) at the time  $t_1$ . Equation (1) then gives the following relations:

$$\begin{aligned}\frac{1}{C_1} &= kt_1 + \text{constant} \\ \frac{1}{C_2} &= kt_2 + \text{constant} \\ \frac{1}{C_2} - \frac{1}{C_1} &= k(t_2 - t_1).\end{aligned}$$

A slight mathematical calculation gives

$$\begin{aligned}\frac{C_1 - C_2}{C_1 C_2} &= k(t_2 - t_1) \\ \text{or } k &= \frac{1}{t_2 - t_1} \cdot \frac{C_1 - C_2}{C_1 C_2}.\end{aligned}$$

Now since  $t_1$ ,  $t_2$ ,  $C_1$ ,  $C_2$  are determined by experiment, we can calculate  $k$ .

If we substitute in this equation (as on page 7)  $A - x_1$  for  $C_1$  and  $A - x_2$  for  $C_2$ , it assumes the following form, which is often found in the literature:

$$k = \frac{1}{t_2 - t_1} \left( \frac{1}{A - x_2} - \frac{1}{A - x_1} \right).$$

Before we describe more closely a specific case illustrating the methods by which such measurements are made experimentally, we note the fact that throughout our discussion of the velocity of chemical reactions we have silently assumed that they all take place at a constant temperature. As we shall see later, temperature exerts a most marked influence upon all chemical reactions; an increase in temperature of  $10^\circ$  causes an acceleration of the chemical reaction of from 200 to 300 per cent. In consequence care must always be taken to keep the heat that is generated during the reaction by the chemical changes themselves as low as possible, in order that its accelerating influence upon the reaction velocity may not prove a source of error.

Besides this, however, the necessary precautions are to be taken to keep the surroundings in which the reaction occurs at a constant temperature. So-called *thermostats* are used for this purpose—apparatus that enable us to maintain constant temperatures for indefinite periods of time. Since such appliances are used in many other investigations of physico-chemical problems, and since they have attained a high degree of perfection within the last few years, I wish to insert a chapter here dealing with these instruments.\*

#### THE MAINTENANCE OF CONSTANT TEMPERATURES.

Baths serve as the most convenient means of maintaining constant temperatures between  $0^{\circ}$  and  $200^{\circ}$ . One of the requirements of these baths is that during indefinite periods of time their temperature must oscillate only between very narrow limits. Between  $0^{\circ}$  and  $50^{\circ}$  the variations in temperature in the apparatus about to be described amount to  $\frac{1}{100}^{\circ}$ ; between  $50^{\circ}$  and  $100^{\circ}$ , about  $\frac{1}{10}^{\circ}$ ; between  $100^{\circ}$  and  $200^{\circ}$ , about  $\frac{1}{5}^{\circ}$ .

In Fig. 1, *AA* is a copper cylinder (height 23 cm., diameter 29 cm.) to which is screwed, by means of the screws *ee*, the rod *a*<sub>1</sub>. This serves as a support for the movable arm *P*, at the end of which is a clamp into which is fastened the copper cylinder *f*, pierced by the shaft *aa*. This shaft has a diameter of 5 mm. and carries the small movable propeller *W* and the movable brass pulley *b*, which by means of a cord *ddd*, connected with the hot-air motor *K*, can be made to rotate rapidly. *R* and *R* are glass windows which enable one to look into (or through) the container *AA*.

\* See C. Geer, *Journal of Physical Chemistry* 6, 85 (1902).

For regulating the temperature the Ostwald toluene regulator (Fig. 2) or the electric regulator (Figs. 3 and 4) may be employed. A constant temperature, accurate to  $0.03^\circ$ , can be obtained with either.

The toluene regulator contains in  $T$  toluene, which for this purpose has been several times distilled from mercury,

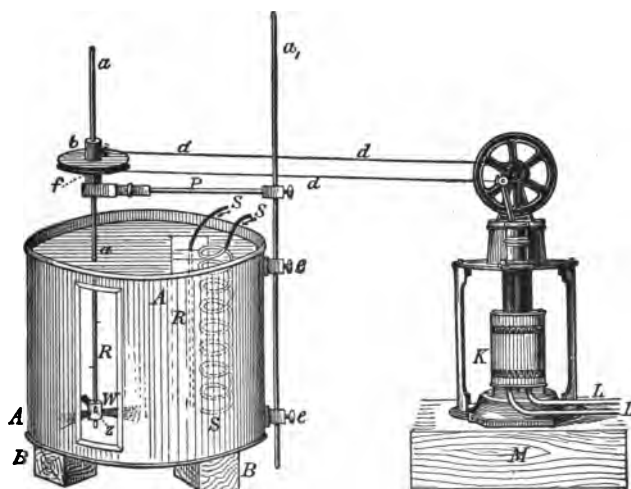


FIG. 1.

and from  $K$  to  $K_1$  mercury. The arrangement of the tubing for conducting gas to and from the apparatus may be seen in the drawing.  $GKK_1T$  is immersed in the thermostat  $AA$  (Fig. 1), until the liquid in  $AA$  reaches the point  $K_1$ ; in other words, deeply enough to have the mercury in the regulator below the surface of the water in the thermostat. The tapering glass tube  $Gd$  is cut off squarely at  $d$ .

If the temperature rises in the thermostat, and if, in consequence,  $d$  is closed by the mercury in the tube  $KK_1$ ,

enough gas continues to flow to the burner through  $t_1 k g t_2 h i$  to keep a small flame lighted. If the temperature falls, the passage  $t_1 b c d$  is again opened, and the flame enlarges. Since the coefficient of expansion of toluol is very great,



FIG. 2.

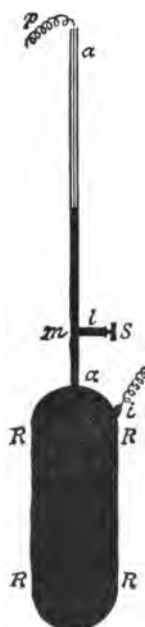


FIG. 3.

the regulator is very sensitive. This instrument is to be used especially when it is desired to keep a constant temperature for long periods of time (days, months, years).

If we wish to work for shorter intervals of time at different constant temperatures, the use of the electric regulator is to be recommended.

The glass vessel *RRRR* (holding from 25 to 40 c.c.) (Fig. 3) is filled with mercury and by means of a copper wire is suspended in the thermostat, so that the mercury in the capillary tube *aa* is just beneath the surface of the water. The platinum wire *i* is fused into the glass and ends in the mercury. Another platinum wire is inserted

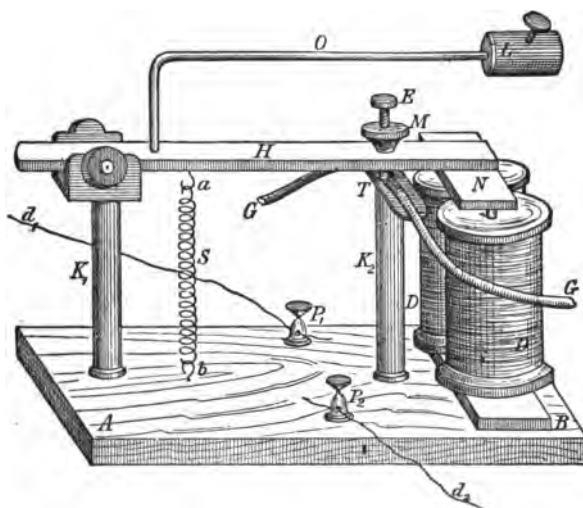


FIG. 4.

so deeply in the capillary tube that at the temperature at which the regulator is to be used it just touches the quick-silver. The height of the mercury meniscus can be regulated at will by means of the screw *S*. Besides the thermostat, the apparatus represented in Fig. 4 is also set up.

The two columns *K*<sub>1</sub> and *K*<sub>2</sub> are screwed into the board *AB*. The lever *H* turns upon *Z*. The end of the lever carries the cross-piece *N*, situated above the two electro-magnets *DD*. If these become magnetised, *N* is

attracted; in consequence the screw  $E$  (kept in position by the set-screw  $M$ ) presses upon and closes the afferent gas-tube  $GG$  lying in the groove  $T$ . By the introduction of a T tube a second path for the gas remains open, so that a small flame is kept burning.

By means of the spiral spring  $S$ , and the movable weight  $L$ , which can be pushed along the bar  $O$ , the pressure upon  $GG$  can be either increased or decreased.

$i$  in Fig. 3 is now connected with one pole of a two-cell storage battery,  $p$  with  $d_1$  of Fig. 4, and  $d_2$  with the other pole of the battery. By moving the wire or turning the screw in the capillary  $aa$ , any constant temperature may be obtained at will.

If electrical energy is at hand, for example in the form of a large storage battery, then by utilising the principle here described, and an incandescent lamp to serve as a source of heat, a simple apparatus may be constructed that has certain advantages over that given here.

The use of the spiral copper tube  $SS$  in Fig. 1 is the following: When the temperature of the room in which the experiment is carried on is high, as, for instance, in summer, it may happen that the tiny flame burning beneath the thermostat, after the regulator has shut off the gas, may still give too much heat to the liquid in the thermostat and so cause its temperature to rise. By connecting the tube  $SS$  with a cold-water tap this difficulty can be overcome.

THE DETERMINATION OF THE VELOCITY OF SAPONIFICATION OF ETHYL ACETATE BY SODIUM HYDROXIDE.

To illustrate the method by which reaction velocity is determined experimentally, we shall describe how the velocity of the saponification of ethyl acetate by sodium hydrate is obtained. We shall consider that we are dealing with the reaction between a  $\frac{1}{4}$  normal ethyl acetate and a  $\frac{1}{4}$  normal NaOH solution at 25°.

To solve this problem we have to determine the concentrations of the NaOH,  $C_1, C_2, C_3, C_4 \dots C_n$ , at the corresponding times,  $t_1, t_2, t_3, t_4 \dots t_n$ ; for if we know these values, then we know the values of all the terms in the equation

$$k = \frac{1}{t_2 - t_1} \cdot \frac{C_1 - C_2}{C_1 C_2}$$

and so know the value of  $k$ .

By means of a pipette, 50 c.c. of a  $\frac{1}{4}$  normal sodium hydrate solution free from carbon dioxide \* are introduced into a Jena-glass flask (of 100 c.c. capacity).

The glass flasks are steamed before using, that is, all the soluble alkali in the glass is dissolved out by a current of steam. This is necessary, because without this precaution the amount of sodium hydrate in the  $\frac{1}{4}$  normal sodium hydrate solution would be increased by an unknown amount.

\* For the preparation and preservation of solutions of caustic soda free from carbon dioxide see J. Spohr, *Zeitschr. f. physik. Chem.* 2, 194 (1888); Paul, *ibid.* 14, 109 (1894); E. Cohen, *ibid.* 37, 69 (1901).



For steaming the flasks we use the apparatus of Abegg, illustrated in Fig. 5. *A* is a flask holding

about 200 c.c. in which water is boiled. The flask is closed with a perforated cork, through which is pushed the funnel *T*. The glass tube *C* is fastened into the neck of the funnel by means of the rubber tube *F*. The flask to be steamed is hung upon the glass tube as indicated in the diagram. The condensed steam containing the alkali collects in the funnel.

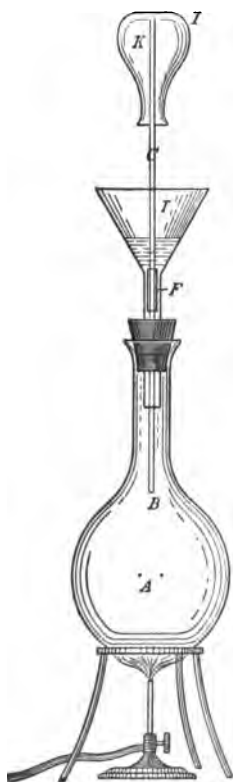


FIG. 5.

The flask containing the  $\frac{1}{10}$  normal sodium hydrate solution is closed with a paraffined cork, weighted with a leaden foot (Fig. 6), and is hung into the thermostat (25°) by means of a copper wire.

A bottle weighted with lead and containing a stock solution of  $\frac{1}{10}$  normal ethyl acetate solution is also hung into the thermostat.

When the solutions have attained the temperature of the thermostat, 50 c.c. of ethyl acetate are removed from the bottle and quickly intro-

duced into the flask containing the NaOH.

The two solutions are thoroughly mixed by shaking. A number of steamed flasks stand ready, into each of which has been measured 10 c.c.  $\frac{1}{10}$  normal nitric acid.

After a certain time, for example two minutes, 10 c.c.

of the mixture are removed from the flask in the thermostat by means of a pipette, and are allowed to flow into the first flask containing the nitric acid. The point ( $t_1$ ) midway between the instant that the mixture of ethyl acetate and sodium hydrate begins to flow into the acid and the instant that the last drop falls into the same is considered the beginning of the reaction time. Time is reckoned by a stop-watch that ticks one-fifth seconds.



FIG. 6.

As soon as the mixture of ethyl acetate and caustic soda flow into the nitric acid, the sodium hydrate still present is neutralised,—the reaction is brought to a stop at the time  $t_1$ . If now, by titration with  $\frac{1}{10}$  normal sodium hydroxide, the excess of nitric acid is determined, we get the concentration ( $C_1$ ) of the caustic soda present in the reaction mixture at the time  $t_1$ .

After another two minutes have elapsed the above process is repeated; we know then the concentration ( $C_2$ ) of the caustic soda in the reaction mixture at the time  $t_2$ . Similarly  $C_3$ ,  $C_4$ , etc., can be ascertained experimentally. By this method the following data were obtained at 25°:

SAPONIFICATION OF  $\frac{1}{10}$  NORMAL ETHYL ACETATE BY  $\frac{1}{10}$  NORMAL SODIUM HYDRATE AT 25°.

$t$ (in Minutes).	$Ct$ (in c.c. $\frac{1}{10}$ normal NaOH).	$k$
2	7.29	.....
4	5.82	6.93
6	4.90	6.77
8	4.18	6.80
10	3.63	6.91
12	3.23	6.89
	Average	$k = 6.86$

If from these figures obtained by experiment the reaction velocity  $k$  is to be calculated, by means of the equation

$$k = \frac{1}{t_2 - t_1} \cdot \frac{C_1 - C_2}{C_1 C_2},$$

it must be noted, first of all, that at the time  $t_1$  ( $= 2$ ) the concentration ( $C_1$ ) in the 10 c.c. of the titrated reaction mixture amounts to  $\frac{7.29}{10}$  of the original concentration ( $\frac{1}{40}$  normal), wherefore

$$C_1 = \frac{7.29}{10} \times \frac{1}{40}.$$

In the same way at  $t_2$  ( $= 4$  minutes)

$$C_2 = \frac{5.82}{10} \times \frac{1}{40}, \text{ etc.}$$

The values of the third column,  $k$ , are therefore calculated as follows:

$$k = \frac{1}{4 - 2} \frac{\frac{7.29}{10} \times \frac{1}{40} - \frac{5.82}{10} \times \frac{1}{40}}{\frac{7.29}{10} \times \frac{1}{40} \times \frac{5.82}{10} \times \frac{1}{40}} = 6.93$$

$$k = \frac{1}{6 - 4} \frac{\frac{7.29}{10} \times \frac{1}{40} - \frac{4.90}{10} \times \frac{1}{40}}{\frac{7.29}{10} \times \frac{1}{40} \times \frac{4.90}{10} \times \frac{1}{40}} = 6.77, \text{ etc.}$$

As the table shows, the mean value of  $k$ , as calculated by this method, is 6.86.

What is the significance of this figure, 6.86, from a chemical standpoint? It shows that if  $\frac{1}{40}$  normal ethyl acetate is saponified by  $\frac{1}{40}$  normal NaOH at 25°, 6.86 mols of the ester are saponified per minute if 1 mol of the ester and 1 mol of the caustic soda are present per litre, and care is taken that the products of the reaction are constantly removed, and the decomposed ester and base are as constantly renewed.

The velocity with which different strong bases, as NaOH, KOH, Ca(OH)<sub>2</sub>, Ba(OH)<sub>2</sub>, Sr(OH)<sub>2</sub>, bring about saponification is, at the same temperature, the same for all. The explanation of this fact will be given later when the theory of electrolytic dissociation is discussed. It will there be seen that it is the so-called OH (hydroxyl) ion, one of the dissociation products in dilute aqueous solution of the bases under consideration, that brings about the saponification.

From these facts it follows that the determination of the velocity of saponification is a general method for determining whether or not certain substances in solution break up into OH ions. In this way, for example, Wys \* has calculated the degree to which water dissociates into its ions, H and OH, and Shields † has investigated the dissociation of salts into free bases and acids,—the so-called hydrolysis of salts. To these phenomena we shall return later.

\* Zeitschr. f. physik. Chem. 12, 514 (1893).

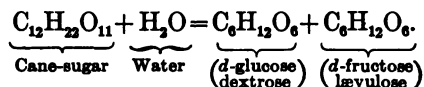
† Ibid. 11, 492 (1893) and 12, 167 (1893).

## SECOND LECTURE.

### The Inversion of Cane-sugar and Catalysis in General.

OF great interest in the study of chemical dynamics and also in the discussion of many physiological problems is the change that cane-sugar suffers under the influence of dilute acids. This problem was exhaustively studied in its dynamical relations as early as 1850 by L. Wilhelmy.\*

If an aqueous solution of sugar is mixed with a dilute acid, a reaction occurs which may be represented by the following equation:



One molecule of cane-sugar yields, upon taking up a molecule of water, one molecule of *d*-glucose and one molecule of *d*-fructose. This chemical change is called *inversion*. It has been found that the acid added undergoes no change in concentration during the reaction.

I should here like to emphasise the fact that the above equation is only a schematic representation of the reaction. The actual mechanism of the inversion is still entirely unknown to us.

The inversion of cane-sugar occurs in a similar manner if the sugar is merely dissolved in water. At room tem-

\* L. Wilhelmy, Ostwald's Klassiker der exakten Wissenschaften 29.

perature, however, the velocity of this reaction (*inversion velocity*) is so low that even after months it is impossible to prove that such a change has actually taken place. If the temperature is raised, the reaction velocity also increases; at 100°, for example, according to the observations of Rayman and Šulc \* an inversion of the sugar can be observed after a few hours.

But the process of inversion and many other chemical reactions are accelerated (or retarded) by the addition of certain substances. (Catalysis, Berzelius.)†

When I call to your attention that C. Ludwig in his *Lehrbuch der Physiologie* thus expressed himself: "It might easily come to pass that physiological chemistry will become a part of catalytic chemistry," and point out that the study of ferments, enzymes, toxines, and modern serum therapy has proved the truth of this remark, it may become evident to you why I undertake at this point a detailed discussion of the subject of catalysis.‡

In harmony with Ostwald we define catalysis as follows: Catalysis is the acceleration (or retardation) of a slowly (quickly) progressing chemical action through the presence of another substance (catalyser or catalytic agent).

It is to be observed that most of these catalysers show two characteristic properties:

1. The mass of the catalytic agent, as compared with the

\* See also Smith, *Zeitschr. f. physik. Chem.* 25, 156 (1898). E. Cohen, *ibid.* 37, 69 (1901).

† See Ostwald: *Dekanatsprogramm der philosophischen Facultät Leipzig 1898*. The same: *Ueber Katalyse. Vortrag gehalten auf der 73<sup>ten</sup> Naturforscherversammlung in Hamburg (Leipzig, 1902)*.

‡ Bredig and Müller von Berneck: *Zeitschr. f. physik. Chem.* 31, 261 (1899); 37, 1 (1901).

mass of the substance acted upon, is in most cases exceedingly small, so that upon this ground alone no further thought need be given to a stoichiometrical chemical reaction between the catalyser and the substance catalysed, even though the degree of acceleration is in most cases clearly and often definitely dependent upon the amount of catalyser present.

2. The catalyser does not itself enter into the reaction, and is therefore often apparently unchanged at the end of the reaction.

In many manuals and text-books the latter property of the catalyser is considered the characteristic feature of catalysis; the most recent investigations have shown, however, that the determining characteristic of this class of effects is to be sought in the acceleration or in the retardation which they bring about in chemical reactions.

The catalytic agent consequently does not initiate a chemical action, which without it could absolutely not occur, but the catalyser alters the velocity of the reaction, which occurs in its absence, only then much more slowly (quickly).

Since in the above equation, representing the process of inversion, two molecules must meet in order that the reaction may occur, it might be assumed that inversion is a bimolecular process. Were this the case, inversion would have to occur according to the equation

$$-\frac{dC_1}{dt} = kC_1C_2,$$

wherein  $C_1$  is the concentration of the cane-sugar, and  $C_2$ , that of the water (see p. 8).

Since the amount of water present in the reaction mix-

ture is, however, very great when compared with the amount of cane-sugar, the change in the concentration of the water during the reaction may be considered as equal to 0, that is to say, the concentration ( $C_2$ ) may be considered as constant. In consequence our equation becomes

$$-\frac{dc}{dt} = kC \quad (1)$$

if we now denote the concentration of the cane-sugar by  $C$ . This equation is, however, the same that we have learned to recognise upon page 5 as representing a monomolecular reaction. In reality, then, inversion proceeds as a monomolecular reaction.

If equation (1) is integrated, we get, according to page 6,

$$k = \frac{1}{t_2 - t_1} l \cdot \frac{C_1}{C_2},$$

or also (according to page 7)

$$k = \frac{1}{t_2 - t_1} l \cdot \frac{A - x_1}{A - x_2}. \quad (2)$$

$k$  is called the *inversion constant*.

If, for example, we wish to determine experimentally the inversion constant of  $\frac{1}{2}$ N.\* hydrochloric acid at 25°, the following method yields the desired result: Purest granulated sugar is dissolved in water † (for example, a 20 per cent stock solution is prepared); in order to prevent the development of bacteria, a little camphor is added to this solution. 10 c.c. of this solution are introduced into two ‡ small steamed (comp. p. 16) flasks, each of which

\*N is the abbreviation for the word *normal*; M for the word *mol* or *gram-molecule*.

† We shall return later, in the discussion of the conductivity of dissolved electrolytes, to the preparation of pure water, such as must be used for this purpose.

‡ As a control, two experiments at least are always conducted under the same conditions.



holds about 25 c.c., and these are hung into a thermostat (Fig. 1) heated to 25°. As soon as the contents of the flasks have assumed this temperature, 10 c.c. of normal hydrochloric acid (which therefore contain 36.46 g. HCl per litre), previously warmed in the thermostat to 25°, are added to the sugar solution in each of the flasks, and the time at which this is done is noted upon a stop-watch ticking one-fifth seconds,—the time ( $t_1$ ). After a certain time, a part of the contents of the first flask is poured into the absolutely dry polarisation tube of a polariscope, the rotation of the solution is determined, and the time necessary to bring about this rotation ( $t_2$ ) is noted. Since the rotation of the invert sugar formed (this is the name given the resulting mixture of *d*-glucose and *d*-fructose) varies with the temperature, the polarisation tube is surrounded by a water-jacket which is kept at a constant temperature. By means of a small suction and force pump the water of the thermostat is made to circulate through this jacket.\*

After the rotation of the solution at the time  $t_2$  has been determined, it is poured back into the flask, which has remained in the thermostat. After some time the determination is repeated (at the time  $t_3$ ), etc.

If we count the time  $t_1$  as the zero point in the experiment (which is to say that at the time  $t_1$  no inversion has as yet occurred, so that the duration of the inversion at this time is zero), then our equation (2) becomes

$$k = \frac{1}{t_2} l \cdot \frac{A}{A - x_2},$$

since  $t_1$  and  $x_1$  (the amount of cane-sugar inverted at the

\* See E. Cohen, *Zeitschr. f. physik. Chem.* 23, 145 (1899).

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time  $t_1=0$ ) both equal zero.\*  $A$  is the concentration of the cane-sugar at the beginning of the experiment;  $x_2$  the concentration of the sugar at the time  $t_2$ .

In this way, for example, in an experiment at  $25^\circ$  the following results were obtained:

INVERSION BY  $\frac{1}{2}$ N. HCl.

$t$ (In Minutes).	Angle of Rotation.	$k$ .
0	25.16	.....
56	16.95	21.80
116	10.38	21.79
176	5.46	21.85
236	1.85	21.85
371	-3.28	22.08
$\infty$	-8.38	.....
	Average †	$k = 21.87$

The angle of rotation at the time  $t=0$  is that of the original sugar solution; the angle at the time  $t=\infty$  is the rotation after complete inversion.

For such acids, as most of the organic, which invert exceedingly slowly, the ultimate rotation angle would be reached only after a very long time (depending upon the temperature at which the inversion takes place),—perhaps after months or years.

But this ultimate rotation may be calculated without great error by utilising the equation of Herzfeld, who upon experimental grounds has proved that each degree of dextro-rotation of the original sugar solution at the

\* A table that simplifies the calculation in no small way is given by Ostwald, Journ. f. prakt. Chemie N. F. 29, 406 (1884).

† To do away with a useless number of zeros, the values of  $k$  in the table were multiplied by 100,000. Thus, for example,  $k = 21.87$  really indicates that  $k = 0.002187$ , etc.

temperature  $t^\circ$ , after complete inversion brings about  $(0.4266 - 0.005 t)$  degrees of lævo-rotation.

Since the concentration ( $A$ ) of the sugar is proportional to the angle of rotation,  $A$  equals  $25.16 + 8.38 = 33.54$ , and  $x_2$  equals  $25.16$  diminished by the rotation angle corresponding to the time  $t_2$ .

So, for example,  $k = 21.79$  (comp. the table) is obtained by the following calculation:

$$t_2 = 116; \quad A = 33.54; \quad x_2 = 25.16 - 10.38 = 14.78.$$

$$k = \frac{1}{116} l \cdot \frac{33.54}{33.54 - 14.78} = \frac{1}{116} l \cdot \frac{33.54}{1876} = \frac{1}{116} l \cdot 1.7878,$$

$$k = 0.002179$$

If we multiply this value by 100,000 to do away with a useless number of zeros, we get the value  $k = 21.79$  of the table.\*

The ordinary apparatus for sugar examination which give the per cent of sugar adapt themselves equally well to the described determinations as those which permit one to read off the rotation angle, since a nearly rigid proportion exists between these angles and the per cent of sugar contained in the solutions.

The investigations that have been made in the manner described have led to the following general results:

1. The inversion velocity, *ceteris paribus*, differs greatly with the character of the acid used for the inversion.

The so-called strong mineral acids all invert with about

\* It is to be noted that  $k$  has here been calculated by Briggs's instead of natural logarithms; since, however, we wish only to prove that the values of  $k$  remain constant, it is permissible in this case, because in this way all the values of  $k$  are changed proportionally.

*INVERSION OF CANE-SUGAR AND CATALYSIS. 27*

the same velocity, while the fatty acids, for example, invert much more slowly.

The following table gives some of the results of Ostwald's\* investigations in this direction with  $\frac{1}{2}$ N. acids. The inversion velocity of hydrochloric acid is taken as equal to 1.

Hydrochloric acid,	1.000	Trichloroacetic acid,	0.734
Nitric acid,	1.000	Dichloroacetic acid,	0.271
Chloric acid,	1.035	Monochloroacetic acid,	0.0484
Sulphuric acid,	0.536	Formic acid,	0.0153
Benzenesulphonic acid,	1.044	Acetic acid,	0.0040

From the fact that all free acids have an inverting action, and that the hydrogen ion is that constituent which all the acids have in common, it has been concluded that this ion is the catalyser in the inversion process. In harmony with this view, experiment teaches that those acids which are most strongly dissociated electrolytically, that is to say, those which contain the largest number of free hydrogen ions in the unit volume, also show the greatest inversion velocity.

In very dilute solutions, according to Palmaer's † observations, the velocity is strictly proportional to the concentration of the hydrogen ions.

We shall later have the opportunity of discussing these facts more fully.

2. In the presence of neutral salts, the inversion velocity is very markedly changed; some salts increase it, others diminish the velocity (Arrhenius, ‡ Spohr §). The cause of this has not yet been clearly explained.

\* l. c.

† Zeitschr. f. physik. Chem. 22, 492 (1897).

‡ Ibid. 1, 110 (1897).

§ Ibid. 2, 194 (1888), where references to the literature may be found.

As we have seen above, the determination of the velocity of the saponification of esters gives us a method for answering the question whether OH ions are present in a given solution, and if so, to what extent. In a similar way, by the inversion of cane-sugar solutions, it can be determined whether H ions are present in a given solution, and if so, to what extent.

Use has been made of this procedure by O. Cohnheim \* for determining the affinity of the albumoses (protalbumose, deutero-albumose, hetero-albumose) and antipeptone for hydrochloric acid.† The following method yielded the desired results. If we invert a certain sugar solution by the addition of a definite amount of hydrochloric acid, then we can determine the reaction velocity of this process at a definite temperature in the above-described manner. If we assume, with Cohnheim, that the velocity is proportional to the concentration of the hydrochloric acid employed, then we know the inversion velocity when the same sugar solution is inverted at the same temperature by a hydrochloric acid having a different concentration. If now albumose or antipeptone is added, the inversion velocity will be diminished in case a part of the hydrochloric acid unites with it, and in this diminution we will have a measure of the amount of hydrochloric acid that has united with the foreign substance added.

\* *Zeitschr. f. Biologie* 33, 489 (1896). F. A. Hoffmann first made use of this method upon Ostwald's suggestion. *Comp. Centralblatt für klinische Medizin* 1889, p. 793 and 1890, p. 521: *Verhandlungen des X. internationalen med. Kongresses* 1890. Abt. 5. *Schmidts Jahrb.* 233, 263 (1892).

† Concerning albumoses, etc., see W. G. Ruppel, *Die Protefne. Beiträge zur experimentellen Therapie von von Behring, Heft 4*, 148-150 (1900).

INVERSION OF CANE-SUGAR AND CATALYSIS. 29

Even though the following calculation is not absolutely correct, we give it here as worked out by Cohnheim.

If the inversion constant of the pure aqueous solution of cane-sugar when inverted by the action of hydrochloric acid is equal to  $k_1$ , then, according to p. 24,

$$k_1 = \frac{1}{t} l \cdot \frac{A}{A - x}, \quad (1)$$

wherein  $t$  represents the duration of the inversion,  $A$  the original concentration of the sugar solution, and  $x$  the amount of sugar inverted at the time  $t$ .

Now if, during the same time  $t$ , the same sugar solution, to which however has been added a certain amount of albumose, is inverted (at the same temperature), the following equation holds for this solution:

$$k_2 = \frac{1}{t} l \cdot \frac{A}{A - x_1}. \quad (2)$$

The value of  $x_1$ , that is the amount of cane-sugar inverted in the solution containing albumose, in the time  $t$ , differs from  $x$ , since the velocities  $k_1$  and  $k_2$  with which the inversion occurs in the two solutions are different.

From equations (1) and (2),

$$\frac{k_1}{k_2} = \frac{l \cdot A - 1 \cdot (A - x)}{l \cdot A - 1 \cdot (A - x_1)}.$$

If now the known amount of free hydrochloric acid in the first solution (1) equals  $B$ , and the unknown amount of free hydrochloric acid in solution (2), which should have the same volume as solution (1), equals  $O$ , then when we set the inversion velocities proportional to the respective concentrations (amounts in the unit volume):

$$\frac{k_1}{k_2} = \frac{B}{O},$$

wherefore

$$O = \frac{k_2}{k_1} B.$$

If, now, it is known how much hydrochloric acid was originally introduced into solution (2), we know, by diminishing this quantity by  $O$ , the amount that has united with the albumose.

If  $g$  grams of albumose and  $s$  grams of hydrochloric acid were present originally in the second solution, then these  $g$  grams of albumose have neutralized  $s - O$  grams of hydrochloric acid.

100 g. of albumose therefore unite with

$$\frac{100}{g} (s - O)$$

grams of hydrochloric acid. In per cent of its weight, albumose consequently unites with

$$z = \frac{100}{g} (s - O) \text{ grams of hydrochloric acid.}$$

If we insert in this equation the value of  $O$  as just found, then

$$z = \frac{100}{g} (s - \frac{k_2 B}{k_1}),$$

from which (2) may be calculated.

A numerical example, taken from Cohnheim's investigations, may serve to illustrate this calculation:

5 c.c. of a 10 per cent cane-sugar solution and 5 c.c. of a hydrochloric acid solution containing 0.05 g. of HCl were introduced into a flask (No. 1).

Into a second flask (No. 2) were introduced 5 c.c. of the same sugar solution and 5 c.c. of a hydrochloric acid solution containing 0.025 g. HCl and 0.25 g. protalbumose.

Both flasks were kept in a thermostat warmed to 40° for four hours; they were then rapidly cooled upon ice, which at once brought the reaction to a stop.\* The rotations of the solutions, which had been ascertained at the beginning of the experiment, were then again determined with the polariscope.

For solution No. 1:  $A = 4.422$ ;  $x = 3.15$ .

From these figures the value of  $k_1$  is calculated by equation (1) upon p. 29:

$$k_1 = 0.541.$$

\* This cooling does not in reality bring the reaction to a complete standstill, but, in consequence of the great lowering of the temperature, the velocity of the inversion is so markedly reduced that in the few minutes necessary to determine the polarisation it cannot noticeably advance.

For solution No. 2 was found

$$A = 4.422; \quad x_1 = 1.135;$$

from which, according to equation (2) upon p. 29,  $k_2$  is calculated:

$$k_2 = 0.158.$$

$$\text{Wherefore} \quad O = \frac{k_2}{k_1} B = \frac{0.158}{0.541} 0.05 = 0.0146.$$

$$s - O = s - \frac{k_2}{k_1} B = 0.025 - 0.0146 = 0.0104.$$

$$z = \frac{100}{0.25} \times 0.0104 = 4.16;$$

that is to say, in the experiment here described the albumose united with 4.16 per cent of its own weight of hydrochloric acid.

In a similar manner it was found that at 40° protalbumose unites upon the average, with 4.32 per cent of its weight of hydrochloric acid; deutero-albumose unites at this temperature with 5.48 per cent, while antipeptone unites with 15.87 per cent of its weight.\*

Bugarszky and Liebermann † have worked upon the same problem, employing, however, an entirely different method, to which we shall return later. These authors express themselves in the following way concerning the experiments of Cohnheim: "The results obtained by Cohnheim with the aid of the sugar-inversion method employed by him, which show that in an aqueous hydrochloric acid solution the velocity of the inversion is diminished through the presence of albumins, permit indeed of the interpretation

\* Through the determination of the velocity of saponification of an ester by sodium hydroxide in the presence of various albumins one could determine in an analogous manner how much sodium hydroxide unites with these substances; this is a problem that has been solved by different means by Bugarszky and Liebermann.

† Pflügers Arch. f. d. ges. Physiologie 72, 51 (1898).

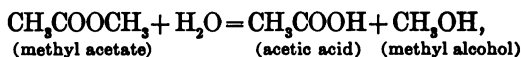


that hydrochloric acid unites with albumins, but may, in part at least, have their origin in the fact that, through the presence of the albuminous substances in the solution, a mechanical hindrance is established which interferes with the free movement of the molecules and consequently diminishes the reaction velocity."

With this remark, which, as will become evident later, has been proved to be not entirely correct (Bugarszky and Liebermann, though through different channels, yet came to the same conclusions as Cohnheim), we enter into a discussion of the

#### DISTURBANCES IN CHEMICAL REACTIONS.

In connection with the remark just cited we ask ourselves first of all: Do chemical reactions proceed in a gelatinous medium with the same velocity as in pure water, or does such a medium act as a mechanical hindrance? This question has been thus decided by Reformatsky: \* The catalysis of methyl acetate, for example, which under the influence of dilute acids takes place according to the following equation:



proceeds with the same velocity in solid agar-agar jelly as in pure water.

As will become evident later, this result is in full accord with the fact that the diffusion of dissolved substances in agar-agar occurs with the same velocity as in aqueous solution, under otherwise similar external conditions.

It was therefore to be expected, *a priori*, that in Cohn-

\* Zeitschr. f. physik. Chem. 7, 34 (1891); comp. also Levi, *De nuovo Cimento* (4) 12, 293 (1900).

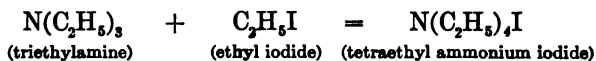
heim's experiments there could be no discussion of a lowering of the reaction velocity in consequence of a "mechanical hindrance."

The results to which Reformatsky's investigations have led are of importance for physiology. Many physiological processes go on in a medium which is not of a purely aqueous nature, but which contains albumin or albuminous substances. Evidently these will have no influence upon the progress of the reaction so long as they do not act chemically upon the reacting substances.

The disturbances which make themselves felt in a reaction may come from widely differing sources.

So, for example, it has developed that in gas reactions (as, for example, in the decomposition of arseniuretted hydrogen, comp. p. 3) the condition (rough, smooth) of the vessel wall exerts a great influence upon the reaction velocity.\* We find ourselves here in a territory which stands in need of more thorough investigation.

The medium in which a reaction that takes place in solution occurs also exerts an important influence upon its velocity. Thus Menschutkin † has proved that the velocity with which the reaction



takes place at 100° in the following indifferent media is a

\* van't Hoff-Cohen, Studien zur chemischen Dynamik, Leipzig 1896, p. 33 et seq., where references to the literature may be found; E. Cohen, Zeitschr. f. physik. Chem. 20, 303 (1896); Bodenstein, ibid. 29, 433 (1899); V. Henri, Journal de physiologie et de pathologie générale, Nov. 1900, p. 933.

† Zeitschr. f. physik. Chem. 6, 41 (1890).

very different one. (The velocity in Hexane is taken as 1 in the table.)

Name of Medium.	Velocity.
Hexane .....	1
Benzol. ....	38.2
Brombenzol.....	150
Acetone .....	337.7
Benzyl alcohol.....	742

The reasons which have thus far been given to explain these differences are not without objection.

In gas reactions the medium seems to exert no influence (Cohen). If, for example, arseniuretted hydrogen is decomposed in the presence of either carbon dioxide or hydrogen, the decomposition proceeds with the same velocity in both instances.\*

\* Zeitschr. f. physik. Chem. 25, 483 (1898).

## THIRD LECTURE.

### The Action of Ferments.

As is doubtless known to you, ferments are divisible into two groups, the *organised* ferments, which are active only during their growth and reproduction, and the *unorganised* or *soluble* ferments,—at Kühne's suggestion called *enzymes*,—which may be extracted from the cells in which they have been formed, and which are able to manifest their characteristic effects outside of the cells also.

The catalytic action of ferments has only within the last few years been thoroughly studied from the standpoint of dynamical chemistry. For our present knowledge concerning this subject we are especially indebted to the observations of Tammann,\* O'Sullivan and Tompson,† Croft Hill,‡ Duclaux and V. Henri.§ Duclaux in his *Traité de Microbiologie* (1899) gives a review of the material at hand.

The inversion of cane-sugar is catalysed (accelerated) not only by weak acids, but also by the enzyme *invertin*

\* Zeitschr. f. physik. Chem. 3, 25 (1889); 18, 426 (1895). Zeitschr. f. physiol. Chem. 16, 269 (1892).

† Journ. of the Chemical Society 57, 834 (1890)

‡ Ibid. 73, 634 (1898). See also Emmerling, Berichte der deutschen chemischen Gesellschaft 34, 600 (1901). C. Oppenheimer, Die Fermente und ihre Wirkungen, Leipzig 1901. Reynolds Green, The Soluble Ferments and Fermentation, Cambridge 1899.

§ Zeitschr. für physik. Chem. 39, 194 (1902). Journal de physiologie et de pathologie générale 3, 875 (1901).

(*sucrase*). From the experiments of O'Sullivan and Tompson, one might think that the laws which govern the inversion of cane-sugar under the influence of this enzyme are almost the same as those that govern the inversion in the presence of dilute acids. The course of the reaction could then be represented by the equation

$$k = \frac{1}{t} l \cdot \frac{A}{A-x}.$$

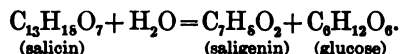
But it will be shown that this equation does not hold under all conditions. On the contrary, the catalysis under the influence of invertin is governed by entirely different and more complicated laws than those that govern the catalysis under the influence of dilute acids. Only when a large amount of ferment is present and the temperature is not very high is the course of the catalysis in the presence of the ferment for a short time similar to the course of the catalysis in the presence of dilute acids. It has been shown that the results obtained by O'Sullivan and Tompson are attributable to the way in which they accidentally arranged their experiments.

But what, now, is the cause of the difference in the inversion process under the influence of the invertin and that of dilute acids? It probably lies in the fact that the ferment undergoes decomposition rather easily. Not only in solution, but in the dry condition also, the ferment suffers (until then unknown) changes which decrease its activity.

Besides this it has been proved that the products formed by the ferment in the catalysed reaction exert an important influence upon the course of the reaction. In

passing it may be pointed out that it has not yet been proved whether the reaction products exert an inhibiting influence primarily, or if a secondary effect is to be attributed to them in that they reduce the activity of the catalyser,—the ferment. An interesting biological field for investigation is therefore open here for the physical chemist.

We shall now direct our attention to a subject that has been closely studied in several directions.\* As may be known to you, the glucosides, such as amygdalin, salicin, helicin, phloridzin, and arbutin, are hydrolysed by emulsin (*symaptase*), that is to say, they break up into simpler products upon taking up water. In the case of salicin the reaction occurs according to the following equation:



While in the inversion of cane-sugar the catalytic agent (the acid) remains unchanged, Tammann has shown that the catalyser—the emulsin—in this case suffers decomposition; this decomposition, into at present entirely unknown decomposition products, proceeds, as experiment has shown, as a monomolecular reaction. The *active mass* (see p. 3) of the emulsin consequently decreases during the hydrolysis of the salicin, and the reaction velocity of the hydrolytic process in consequence also decreases.

Now, in general, if the amount of ferment added is large and the temperature is low, it may happen that the decomposition velocity of the ferment is so slight when compared with the velocity with which the salicin is decomposed, that the change in the active mass of the ferment may apparently have no influence upon the velocity of the

\* Tammann, *Zeitschr. f. physik. Chem.* 18, 426 (1895).

decomposition of the salicin. This was the case in the experiments of O'Sullivan and Tompson, in which the invertin suffered only a slight decomposition. Because of this accidental condition of affairs it seemed as though the reaction which they studied progressed as a monomolecular one.

If, further, we remember that the reaction products (*d*-glucose and *d*-fructose) have no influence upon the velocity of the inversion of cane-sugar by dilute acids, while they often have a marked effect upon the velocity of inversion when this is accelerated by ferments, it becomes intelligible why the process of taking up water under the influence of ferments runs a totally different course from that under the influence of dilute acids.

How great the inhibiting effect of the reaction products may be is shown by the following experiment: After a certain amount of salicin had been hydrolysed at 26° by emulsin, the reaction came to a standstill when 83 per cent of the salicin had been decomposed. However, after one of the reaction products, the saligenin, was removed by shaking out with ether, the reaction recommenced, and after twenty-four hours the entire amount of salicin originally present was decomposed.

The inhibiting influence of the reaction products can also be shown in a somewhat similar way by making two experiments, in the first of which, *ceteris paribus*, the ferment is mixed with the substance to be decomposed, while in the second a certain amount of the reaction products is previously added; it is then seen that in the latter the reaction from the start progresses more slowly than in the first-described instance. In consequence of the inhibiting influence of the reaction products, ferment-

tations show a *limit*; the reaction does not progress entirely to an end, but comes to a standstill even though a certain amount of substance which could be decomposed by the ferment is still present.

The point at which this limit is reached is dependent upon the amount of ferment added originally, and upon the temperature.

That a limit must be reached in the action of ferments which suffer a decomposition in the course of the reaction which they catalyse—that, in other words, even when a large amount of the ferment is present and its action is allowed to go on indefinitely, a certain amount of the substance undergoing decomposition under the influence of the ferment must remain unaltered—may be shown in the following way (Tammann).

If  $A$  is the amount of ferment originally present,  $B$  the amount of substance the decomposition of which is catalysed by the ferment,  $x$  the amount of the ferment which at the time  $t$  becomes inactive, and  $y$  the amount of substance which at this time has been decomposed, then, since the reaction velocity at the time  $t$  is proportional both to the concentration of the substance undergoing decomposition and to the concentration of the ferment (Guldberg and Waage, see p. 3),

$$\frac{dy}{dt} = k(A - x)(B - y) \quad (1)$$

Herein  $k$  is the velocity constant of the fermentation process, that is to say,  $k$  indicates the velocity with which, for example, the salicin is decomposed, for  $(A - x)$  and  $(B - x)$  are the concentrations of the ferment and of the substance undergoing decomposition at the time  $t$ .

We have already pointed out that the decomposition of the ferment progresses as a monomolecular reaction, hence for this part of the reaction the following formula holds:

$$c = \frac{1}{t} l \cdot \frac{A}{A - x}, \quad (2)$$

wherein  $c$  is the velocity constant of the decomposition which the ferment (for example, emulsin) suffers in aqueous solution. If now, we determine the value of  $(A - x)$  of equation (2) and insert



this in equation (1), and if we remember that (2) may also be written

$$e^{ct} = \frac{A}{A-x},$$

$$A-x = \frac{A}{e^{ct}},$$

wherein  $e$  is the unit of the Napierian system of logarithms (2.7182...), then equation (1) assumes the following form:

$$\frac{dy}{dt} = \frac{kA}{e^{ct}} (B-y),$$

or  $\frac{dy}{B-y} = \frac{kA}{e^{ct}} dt.$

By integration,

$$l. \frac{B-y}{B} = -\frac{k}{c} A \left(1 - \frac{1}{e^{ct}}\right).$$

By this equation can now be determined how much substance ( $y$ ) is decomposed by the ferment in the time  $t$ , when the amount of the ferment ( $A$ ) originally present and the amount of substance undergoing decomposition ( $B$ ) is known, and the decomposition velocity ( $c$ ) of the ferment and the velocity ( $k$ ) with which the substance is decomposed under the influence of the ferment at a definite temperature are also known.

If in this equation we make  $t = \infty$ —that is, if we ask how much substance is decomposed by the ferment in infinite time—then, since  $\frac{1}{e^{ct}}$  becomes equal to 0, we find that

$$l. \frac{B-y}{B} = -\frac{k}{c} A, \quad (a)$$

wherefore

$$e^{-\frac{k}{c} A} = \frac{B-y}{B},$$

or  $\frac{1}{e^{\frac{k}{c} A}} = \frac{B-y}{B},$

$$y = B - \frac{B}{e^{\frac{k}{c} A}}.$$

Or to express this in words: The amount of substance ( $y$ ) decomposed even after infinite time never equals the amount originally

present ( $B$ ), but is always less, for  $B$  must always be diminished by a certain value,  $\frac{B}{\frac{k}{e} \cdot A}$ . It can therefore be seen that a certain

part of the substance originally present remains undecomposed—that a limit exists which can never be exceeded. The experiments of Tammann corroborate this conclusion.

Of great interest are the analogies recently discovered by Bredig and Müller von Berneck \* between the action of enzymes and the action of a number of colloidal solutions of metals (*sols*), which have led these observers to give the name of *inorganic ferments* to these substances.

Since these observations are also of great importance in showing the way in which dynamical studies on the effects of ferments are to be made in the future, I wish to consider the results thus far obtained in some detail.

It had long been known that a large number of diastatic reactions are accelerated not only through the addition of ferments, but also through the addition of finely divided metals (such as platinum, iridium, and silver). The decomposition of hydrogen peroxide into water and oxygen is as strongly catalysed by platinum, gold, silver, iridium, and many metallic oxides as by fibrin. Schönbein † found, moreover, that all organic ferments, such as diastase, emulsin, myrosin, yeast, and many watery extracts of plants bring about similar effects. Concerning these Schönbein says: "It seems to me to be a most noteworthy fact that

\* Zeitschr. f. physik. Chem. 31, 258 (1899); Bredig and Ikeda, *ibid.* 37, 1 (1901); Zeitschr. f. Electrochemie 7, 161 (1900). Bredig and Reinders, *ibid.* 37, 323 (1901). See also G. Bredig, *Anorganische Fermente*, Habilitationsschrift, Leipzig 1901, where full references to the literature may be found. McIntosh, *Journal of Physical Chemistry* 6, 15 (1902). Billitzer, *Berichte der deutschen chemischen Gesellschaft* 35, 1929 (1902).

† *Journ. f. prakt. Chem.* (1) 89, 32 and 325 (1863).

all the given ferment-like or catalytically acting substances should possess the power of decomposing hydrogen peroxide in a manner similar to that of platinum, a coincidence in different activities which must give room to the suspicion that they have their foundation in similar causes." And, further, after he too has foreseen an analogy between the action of the platinum and the action of the ferments: "The results of my latest investigations have strengthened my old, oft-repeated suspicion, that the dissociation of hydrogen peroxide through platinum is the prototype of all fermentations, and have made me willing to extend in general the interpretation which I have given of the above process to all catalytic phenomena."

Through Bredig's observations on the electrical pulverisation of metals it has become possible to produce so-called *colloidal solutions* (pseudo-solutions, sols) of metals of great purity, in which the amount of the metal present can be determined quantitatively.

If, for example, we wish to make the so-called platinum solution of Bredig, the platinsol, the following method can be used:

To the binding-posts of an electric circuit (for example 70 volts) are connected in series (Fig. 7), the ammeter (*A*), an adjustable resistance-box (*W*) (a battery of lamps or a fluid resistance), which with a difference of potential of 70 volts yields 5-10 amperes, and two electrodes *G*, made of platinum wires about 2 mm. in diameter and 6-8 cm. long. The one platinum wire is pushed through a narrow glass tube *r* (Fig. 8), so that the electrodes may be handled. The resistance is adjusted until, upon closing the circuit and carefully separating the electrodes under water, whereby a small arc about 1 mm. long is produced, one

obtains the desired strength of current. The sol is then prepared as follows: A glass dish *S*, of about 50–100 c.c. capacity, and cooled externally by ice, is filled with very pure distilled water,\* free from carbonic acid. The electrodes are then grasped in the hands, brought into the

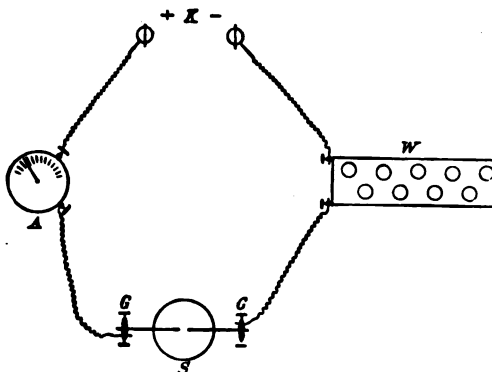


FIG. 7.

position shown in Fig. 8, and the circuit is closed between their tips 1 to 2 cm. below the surface of the water. The tips are slowly separated, for about 1 to 2 mm., whereby a tiny arc light is formed. As long as the arc hisses quietly, the platinum emanates in deep brown clouds from the cathode, and distributes itself partly as a sol, partly in coarser particles throughout the surrounding fluid. The arc is easily extinguished. When this happens the current is again closed, and the operation is repeated, with occasional stirring, until the water in the dish is converted into a dark fluid. Overheating is carefully to be avoided, and the experiment must not be continued too

\* See foot-note on p. 23.

long with a single dish of water, as otherwise the platinsol coagulates easily. The coarser platinum particles are filtered off, when a fluid is obtained in which the platinum remains suspended for months.

Now such a sol, which is nothing but a mechanical suspension of exceedingly fine particles of the given metal in water, like certain organic ferments, acts as a powerful catalytic agent in bringing about the decomposition of  $H_2O_2$  into water and oxygen—a decomposition that occurs also without the addition of this substance, only then much

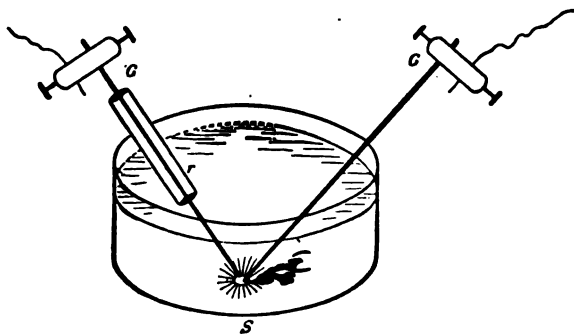
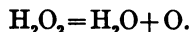


FIG. 8.

more slowly (see p. 21). The velocity of this decomposition under different conditions has been measured by Bredig and Müller von Berneck. All the measurements were made in a thermostat at constant temperature; the concentration of the sol was determined by gravimetric means; that of the hydrogen peroxide solutions by titration with potassium permanganate.

In order not to weary you with superfluous data, I shall give here only the most important results of these investigations.

1. The decomposition of the hydrogen peroxide is a monomolecular reaction, and consequently proceeds according to the equation



The addition of even exceedingly small amounts of platinum accelerates the reaction very perceptibly; one gram-atom of platinum (194.8 g.) diluted to seventy million litres still has a definite catalytic effect upon more than a million times its amount of hydrogen peroxide. One cubic centimetre of the solution which still showed a demonstrable catalysis therefore contained  $\frac{1}{300000}$  milligram of platinum. The fact that such an exceedingly small amount of substance can exert a clearly demonstrable influence upon the course of a reaction brings to mind the recent investigations of Gautier,\* who found that about 0.17 milligram of arsenic is present in the thyroid gland of the healthy individual. The presence of this small amount, being about  $\frac{1}{4000000}$  of the total body weight, seems to be necessary for the general well-being of the individual. The words of Gautier, "car pas de thyroïde sans arsenic et pas de santé sans thyroïde" (for there is no thyroid without arsenic, and no health without a thyroid), assume a deep significance in the light of the observations of Bredig and Müller von Berneck.†

Into this category fall also the exceedingly interesting

\* Compt. rend. 129, 929 (1899). See also Bulletin de l'Acad. d. Médecine, No. 32 (1900); B. Moore and C. O. Purinton, Über den Einfluss minimaler Mengen Nebennierenextrakts auf den arteriellen Blutdruck. Pflügers Arch. 81, 483 (1900).

† The correctness of Gautier's results has been questioned. See Hödlmoser, Zeitschr. f. physiolog. Chem. 33, 329 (1901), and K. Cerný, *ibid.* 34, 248 (1902).

observations of Nägeli \* upon oligodynamical phenomena, which were not made public until Schwendener published them after Nägeli's death.

Nägeli found that exceedingly small amounts of metals (or metallic salts) dissolved in water have a distinctively toxic effect upon certain living cells.

It was found, for example, that spirogyra cells are poisoned by water in which one part of copper is present in 1000 million parts of water. These experiments have been repeated and corroborated by Cramer,† Dehérain and Demoussy,‡ and by Coupin.§

The question as to whether these facts, as some affirm, give support to the teachings of homœopathy may for the time being be set aside.||

2. The catalytic activity of the platinsol is often greatly decreased through the addition of even very small amounts of electrolytes (salts, acids, etc.).

Thus the velocity constant which in a given case had been 0.023 originally, fell to 0.015 when  $\frac{1}{5000}$  mol  $\text{Na}_2\text{HPO}_4$  was added to each litre of the  $\text{H}_2\text{O}_2$  solution. When the experiment was repeated several days later with the same solution of platinum, which had in the mean time remained in contact with the sodium phosphate, it was found that the constant had decreased still more (0.011).

This progressive loss in the activity of the catalytic

\* Neue Denkschriften der allgemeinen schweizerischen Gesellschaft für die gesammten Naturwissenschaften 33, Abt. 1 (1893). See also H. de Varigny, Revue Scientifique 30, 2, Sept. 1893.

† Ibid.

‡ Compt. rend. 137, 523 (1901).

§ Ibid. 132, 645 (1901).

|| v. d. Stempel, Geneeskundige Courant (Amsterdam); April 14, 21, and May 5, 1901.

agent brings to mind the phenomena of which we have already spoken in dealing with ferments. In the case of the platinsol the reason for this progressive loss in activity is found in the fact that the platinum in the colloidal solution is precipitated by the addition of electrolytes, and that in consequence it can no longer take part in the given reaction.

Since this "salting out" of the platinum is also brought about through the presence of slight traces of electrolytes in the water of the sol, especial stress is to be laid upon the great purity of the water used in making these colloidal solutions.

3. The velocity with which the catalysis of the hydrogen peroxide occurs in the presence of the sol increases with the concentration of the platinum. Yet different, equally concentrated solutions of platinum do not always give the same result. As with organic ferments, the activity is dependent upon the mode of preparation, upon the age, in general upon the *history* of the given preparation. If this is the same for two solutions, then the activity of the two is also the same.

4. In one particular the behaviour of the platinum solution of Bredig deviates markedly from that of the organic ferments. While the latter reach a so-called *limit* (p. 39) in their activity, that is to say, while the reactions that are catalysed by organic ferments are incomplete, the catalysis of hydrogen peroxide under the influence of the platinsol is complete. The catalysis of the hydrogen peroxide behaves, therefore, like the inversion of cane-sugar under the influence of dilute acids. The decrease in the activity of the colloidal platinum takes place so slowly, compared with the great velocity with which the hydrogen



peroxide decomposes, that the activity of the platinum remains apparently constant.

5. Of exceedingly great interest is the parallelism that exists between the platinsol and the organic ferments in their sensitiveness to certain paralysing substances.

The activity of all organic ferments that catalyse the decomposition of hydrogen peroxide is paralysed by many reagents. In the case of platinsol we also find these "*phenomena of intoxication.*" Yet just as the organic ferments after a certain time *recover* from the intoxication, and can then catalyse anew, the platinsol recovers from its intoxication.

The cause of this peculiar behaviour has not yet been explained. The organic as well as the inorganic ferments are very sensitive to prussic acid. One mol HCN in twenty million litres (0.0014 mg. HCN per litre) is sufficient to decrease the velocity of the catalysis one half. Sulphuretted hydrogen is also very poisonous. It is a remarkable fact that the hæmic and respiratory poisons, prussic acid and hydrogen sulphide, should be the ones to act as paralytic agents. The same phenomena are observed with goldsol as with platinsol.

6. The order in which the  $H_2O_2$  and the HCN are added to the catalytic agent, that is to metallic sol, has an important effect upon the degree of paralysis produced.

If blood or organic ferments are used as catalytic agents, the influence of the order in which these substances are added to each other is manifest in this case also.

The paralysis produced by the catalyser is always greater when the prussic acid is added first and then the  $H_2O_2$ , than when the reverse order is followed. The explanation of these puzzling phenomena is still lacking.

I must not omit to mention that the results communicated to you have been obtained through strictly quantitative methods of measurement such as modern chemistry has given us. It is to be greatly regretted that Jacobson,\* for example, in his interesting studies upon enzymes did not make use of these methods. In the repetition of these experiments in the manner here described, an interesting physico-chemical field is opened for the labours of the biologist.

I would very much like to discuss with you further questions bearing upon our knowledge of the ferments, yet I must content myself with pointing out that, by studying the admirable work of Duclaux to which reference has been made above, an abundance of questions will arise the solution of which seems possible by utilising the methods that have been here described.

\* *Zeitschr. f. physiol. Chem.* 16, 340 (1899).

## FOURTH LECTURE.

### The Influence of Temperature upon Reaction Velocity.

UNTIL now we have only discussed the course of chemical reactions at constant temperature. We shall now study the question, What influence has temperature upon the velocity of chemical reactions?

The experiences of daily life indicate that a rise in temperature is followed by a rise in the reaction velocity. We have but to think of the rapid decomposition of foodstuffs, or of the rapid decomposition of corpses in summer or in the tropics; or of the use of ice where we wish to inhibit the velocity of such processes (the cold storage of foodstuffs, the use of ice-bags in inflammations).

If we wish to determine the influence of temperature upon a reaction, we must study the course of the reaction at various temperatures in the thermostat, and determine the velocity constant belonging to each temperature.

A simple relation has been shown by van't Hoff to exist between the velocity constant of a reaction and the absolute temperature (that is, temperature reckoned from  $-273^{\circ}$  C. as the zero point) at which it takes place.

Arrhenius has proved that this relation may in many cases be represented by the following formula:

$$l \cdot k = -\frac{A}{T} + \text{constant.}$$

**TEMPERATURE AND REACTION VELOCITY. 51**

Herein  $k$  is the velocity constant of the reaction at the absolute temperature  $T$ , and  $A$  is a constant.

If the velocity constants  $k_1$  and  $k_2$  of any reaction are determined at the two temperatures  $T_1$  and  $T_2$ , two equations are obtained:

$$l \cdot k_1 = -\frac{A}{T_1} + \text{constant} \quad (1)$$

and 
$$l \cdot k_2 = -\frac{A}{T_2} + \text{constant}, \quad (2)$$

from which the two unknown values  $A$  and constant can be calculated. If these are known, then the unknown velocity constant  $k_3$  at the temperature  $T_3$  may be calculated in advance from the equation

$$l \cdot k_3 = -\frac{A}{T_3} + \text{constant},$$

for in this equation  $A$  and the constant are known.

The following example, which deals with the influence of temperature upon the velocity of the saponification of ethyl acetate by sodium hydroxide, may illustrate the use of the formulæ.

Warder\* found this velocity to be 1.92 at 7.2° and 10.92 at 34.0°. Suppose the velocity at 30.4° were to be determined.

From equations (1) and (2) we calculate first of all the value of  $A$  and the constant. We get for 7.2°—according to the absolute temperature scale  $7.2 + 273 = 280.2$ —

$$l \cdot 1.92 = -\frac{A}{280.2} + \text{constant}. \quad (1a)$$

In a similar way we get for 34.0°—according to the absolute scale  $34.0 + 273 = 307$ —

$$l \cdot 10.92 = -\frac{A}{307} + \text{constant}. \quad (2a)$$

\* Berich. der deut. chem. Gesellschaft 14, 1365 (1881).

From equations (1a) and (2a) we calculate the two unknown values  $A$  and constant:

$$l \cdot 10.92 - l \cdot 1.92 = \frac{A}{280.2} - \frac{A}{307}. \quad (3)$$

Since for convenience we are working with Briggs's logarithms, we must multiply the first member of equation (3) by 2.3025, in order to reduce the natural to Briggs's logarithms.

$$2.3025 (\log 10.92 - \log 1.92) = \frac{26.8}{280.2 \times 307} A,$$

$$2.3025 \times 0.75492 = \frac{26.8}{86021} A,$$

$$A = 5579.$$

If we introduce this value of  $A$  into equation (2a), we find

$$l \cdot 10.92 = -\frac{5579}{307} + \text{constant},$$

$$\text{Constant} = 18.17 + 2.392 = 20.562.$$

The equation which represents the velocity of the reaction studied by Warder at all temperatures consequently assumes the following form:

$$l \cdot k = -\frac{5579}{T} + 20.562.$$

For  $30.4^\circ$  ( $T = 273 + 30.4 = 303.4$ ) we get

$$l \cdot k = -\frac{5579}{303.4} + 20.562,$$

$$k = 8.82,$$

while actual experiment gave 8.88 for the value of  $k$ .

## TEMPERATURE AND REACTION VELOCITY. 53

The following table shows how well the above formula adapts itself to the calculation of the reaction velocity at various temperatures.

Temperature.	$k$ (observed).	$k$ (calculated).
3.6°	1.42	1.48
5.5	1.68	1.70
11.0	2.56	2.51
12.7	2.87	2.82
19.3	4.57	4.38
20.9	4.99	4.86
23.6	6.01	5.78
27.0	7.24	7.16
28.4	8.03	7.81
30.4	8.88	8.82
32.9	9.87	10.24
35.0	11.69	11.60
37.7	13.41	13.59

The influence of temperature between 0° and 200° has been investigated in very many reactions. These have shown that through an increase in temperature of 10° the reaction velocity is increased two- or threefold.

In determining the velocity of a reaction at any (constant) temperature, great importance is therefore to be attached to the maintenance of a constant temperature, for changes in temperature exert an enormous influence upon the course of a reaction. This explains the use of thermostats, which prevent any great changes in temperature (see p. 10).

Many reactions proceed very slowly under the conditions at which they occur in daily life—at temperatures between 0° and 25°; so slowly, indeed, that with our ordinary analytical means we can demonstrate no changes in the systems in which these reactions take place.

Because of this it has been believed that no change what-

soever occurs in such cases; but that a reaction does actually take place, the velocity of which is, however, very low, can be proved by watching the reaction a sufficiently long time. The reaction products are then increased in amount, and finally fall within the sphere of our measurable analytical reactions.

Our phosphorus matches actually burn up if we keep them in their boxes. The rapidity with which the combustion proceeds is, however, under ordinary circumstances, so slight that we can observe no change in them even after a very long time. If we raise the temperature by striking the matches on a rough surface, the combustion velocity rises because of the local rise in temperature, and rapid oxidation sets in. The heat generated in this process heats the neighbouring phosphorus particles to so high a temperature that the oxidation velocity becomes very great there too, and the match catches fire.

If reactions which we wish to use for analytical purposes occur too slowly at ordinary temperature, we simply raise the temperature. The inversion of 9.5 g. cane-sugar by  $\frac{1}{4}$  N. hydrochloric acid as used in the sugar determination method of Soxhlet would, for example, require many days at room temperature. By warming the reaction mixture to 100° complete inversion is brought about within half an hour. Conversely, the reaction velocity between sodium and hydrochloric acid, which at room temperature is enormous, can be reduced to such an extent by cooling to -80° that it can be followed quantitatively (Dorn and Völlmer \*).

As was shown above, ferments catalyse many chemical

\* Wiedemanns *Annalen der Physik und Chemie*, Neue Folge, 60, 468 (1897). See also Pictet, *Compt. rend.* 115, 814 (1892).

reactions. What influence, now, has temperature upon such catalytic activities?

A great difference exists between the influence of temperature upon purely chemical reactions and those in which ferments play a rôle.

While the formula

$$l \cdot k = \text{constant} - \frac{A}{T}$$

shows that with a rise in temperature, that is with an increase in the value of  $T$ , the value of  $l \cdot k$  and consequently of  $k$  becomes progressively greater,\* this is not the case in reactions in which ferments take part. Here also we find a region in which the reaction velocity is increased by an increase in the temperature, yet this increase is not without limit. A temperature is finally reached at which the reaction velocity attains a maximum, after which a further increase in temperature diminishes the velocity. If the temperature is raised still higher, the velocity finally falls to zero, that is to say, the reaction comes to a standstill.†

This behaviour is represented graphically in Fig. 9, in which the abscissas indicate the temperatures, the ordinates the reaction velocities, of the action of *indigo enzyme* obtained from *Indigofera leptostachya* (curve 1), from *Polygonum tinctorium* (curve 2), from *Phajus grandiflorus* (curve 3), from *Saccharomyces sphaericus* (curve 4), and

\* Conversely, by lowering the temperature,  $k$  becomes steadily less. If  $T = 0$ , that is at absolute zero ( $= -273^\circ$ ), then  $l \cdot k = -\infty$ , and the reaction velocity  $k = 0$ .

† The temperature at which the reaction velocity reaches its maximum is generally called by biologists the optimum temperature of the given reaction, while by the maximum temperature is understood the temperature at which the reaction no longer takes place.



*emulsin* (curve 5) from sweet almonds, upon indican, which is thereby broken up into indoxyl and glucose (Beyerinck \*). In general, it is found that the curves of all ferments have a similar form.

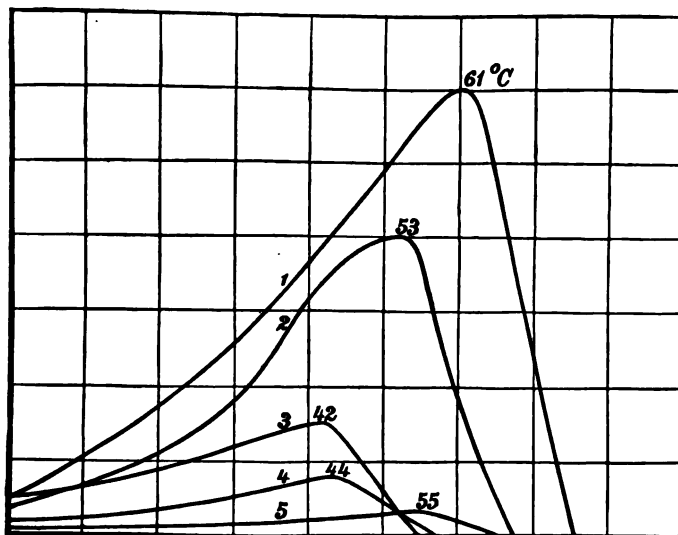


FIG. 9.

The temperature for the maximum velocity of any given ferment is not always the same, but is dependent upon the properties of the medium in which the ferment acts.

Why is a maximal velocity reached? The answer to this question is found in the decomposition which the ferment suffers upon an increase in the temperature. We have already discussed this in the case of *emulsin* (see p. 37).

\* Verslagen der Kon. Akad. van Wetenschappen te Amsterdam, 8, 572 (1900).

If, for example, a watery solution of salicin and emulsin were heated together, and the ferment remained constant in its action, the reaction velocity would progressively increase with an increase in temperature, just as in the case of the inversion of cane-sugar by dilute acids. The ferment, however, suffers decomposition at the same time, and the rapidity of this decomposition increases in a similar way with an increase in temperature. The product of these simultaneously occurring reactions will be represented by a curve which attains a maximum at one point. This experiment shows to be indeed the case.

Now, since the two reactions, the joint effects of which yield this curve, have their individual characteristics, which in part depend upon the properties of the medium in which the reaction occurs, it can readily be seen that the maximal velocity may not always be reached at the same temperature even for one and the same ferment.

Utilisable data on the influence of temperature upon fermentation are very scanty.\* According to Tammann's † observations the velocity with which emulsin undergoes decomposition above 60° when in aqueous solution may be fairly well represented by the formula of van't Hoff-Arrhenius. If, from this equation, the decomposition velocity at 75° is calculated from the velocities observed at 60° ( $k=0.80$ ) and 70° ( $k=5.9$ ), it is found that  $k=14.7$ . Actual experiment yields 15.3 for the value of  $k$  at 75°.

These figures also show what an enormous influence a rise in temperature has upon this decomposition, for the velocity of the decomposition rises above sevenfold by an increase in temperature of 10°.

\* Duclaux, *Traité de Microbiologie* T. II, 174 (1899).

† *Zeitschr. f. physik. Chem.* 18, 426 (1895).

A continuation and amplification of the experiments of Tammann are greatly to be desired, in order to discover the principles that underlie the action of various ferments.

The fermentative action of platinum in the decomposition of hydrogen peroxide is governed, at not too high temperatures, by the same laws that govern simple chemical reactions. The influence of temperature may be represented by the van't Hoff-Arrhenius formula.

This fact becomes intelligible when we remember that the progressive decrease in the activity of the colloidal platinum through heat when compared with the great rapidity of the decomposition of the  $H_2O_2$  is so slight that the active mass of the platinum may be regarded as constant during the reaction. If the colloidal platinum were as sensitive to an increase in temperature as the ferments, a maximal velocity would be found in the catalysis of hydrogen peroxide in the presence of this inorganic ferment also. Such a maximum has indeed been proved to exist by C. Ernst\* in the case of the decomposition of oxy-hydrogen gas in water in the presence of colloidal platinum.

Indeed the investigations of Bredig and Müller von Berneck have already rendered it probable that if the colloidal platinum and the hydrogen peroxide solution were together heated more strongly, a temperature at which the reaction velocity shows a maximum would be found here also.

Since numerous chemical changes take place in the animal and vegetable body, the question arises: What influence has temperature upon these chemical changes and upon the phenomena of development which are closely associated therewith?

\* *Zeitschr. f. physik. Chemie* 37, 448 (1901).

The changes going on here are naturally of a much more complicated order than those that occur *in vitro*, and the discovery of the laws that govern them is consequently accompanied by considerable experimental difficulties.

Let us consider, first of all, the investigations that aim to illustrate the influence of temperature upon the rapidity of the development of plants.\*

In the experiments upon plants, in which an increase in the length of certain parts of the plant in the unit of time was chosen as a measure of development, it soon became evident that the rapidity of development when graphically represented as a function of the temperature furnishes a curve which is analogous to that with which we have become acquainted in the action of ferments. The rapidity of development at first increases with an increase in temperature, passes through a maximum, and falls finally to zero. Here also the temperature of maximal velocity varies, being different for each plant species.

There is often given in botanical literature a low temperature limit at which the growth of plants is supposed to cease suddenly. But it is always pointed out in these investigations that death occurs only at a temperature a few degrees below this.

From what we know in general of the course of reactions at low temperatures, there seems to me to be no reason for assuming the existence of a temperature limit at which growth ceases suddenly. Much more probably we are dealing with a very slow rate of growth which can be measured only by observations extended over long periods of time.

\* For references to the literature, see among others A. B. Frank, *Die Krankheiten der Pflanzen* (Breslau 1895, Trewendt) p. 216.

The quantitative determinations on the influence of temperature upon the development of plants as found in the literature are, in general, not sharply defined; the temperatures at which the observations have been made show considerable variations. Now, since only a fleeting glance suffices to show that changes in temperature exert here also a great influence upon the velocity of development, particularly within those temperature limits which are most like the conditions under which these plants exist in nature, it will be readily appreciated that the data obtained in this way are full of great errors and are not fit for further consideration.

Yet in a few cases almost as great an influence of temperature as in simple chemical reactions may be proven to exist.

Careful experiments have been made by Clausen \* to determine the influence of temperature upon the excretion of carbon dioxide by bean-germs, wheat-germs and syringa-buds; variations in temperature did not exceed  $0.2^{\circ}$  in these experiments. The results of Clausen's experiments are given in the table on the opposite page. The figures in the second, third, and fourth columns give the amounts in milligrams of carbon dioxide exhaled by the given plants (100 g.) per hour.

We see that even at  $0^{\circ}$  a not inconsiderable amount of carbon dioxide is given off by all of the plants experimented upon. Indeed respiration must occur even below  $0^{\circ}$ , "and it can scarcely be doubted that it does not cease until the plant freezes."

The table shows that here also the velocity attains a

\* *Landwirtschaftliche Jahrbücher* 19, 893 (1890), where references to the literature may be found.

TEMPERATURE AND REACTION VELOCITY. 61

maximum, after which with a further increase in temperature it again falls.

Temperature.	Wheat-germs.	Bean-germs.	Syringa-buds.
0°	7.27	10.14	11.60
5	13.86	18.78	19.93
10	18.11	28.95	30.00
15	34.37	45.10	48.45
20	43.55	61.80	78.85
25	58.76	86.92	93.30
30	85.00	100.76	108.00
35	100.00	108.12	146.76
40	115.90	109.90	176.10
45	104.45	95.76	164.10
50	46.20	63.90	152.80
55	17.70	10.65	44.00

If we consider the increase in the velocity between 0° and 25°, we find that the amount of carbon dioxide expired increases in all cases about 2.5-fold, with an increase in temperature of 10°. This increase is therefore as great as that in simple chemical reactions (see p. 51).

According to Oscar Hertwig,\* frog's eggs are much better adapted to experiments on the influence of temperature upon the rate of development of living organisms than plants or germinating seeds such as are often employed by plant physiologists in such investigations.

Hertwig has made an extensive study of the influence of temperature upon the rapidity of the development of the eggs of *Rana fusca* and *Rana esculenta*.

Even though the temperature was not kept absolutely constant in these experiments, the variations were not very great, so that the data obtained by Hertwig permit of closer quantitative consideration.

\* Arch. f. mikroskop. Anat. u. Entwicklungsgesch. 51, 319 (1898).

In Fig. 10 is represented graphically the rate of development of frog's eggs as a function of the temperature.

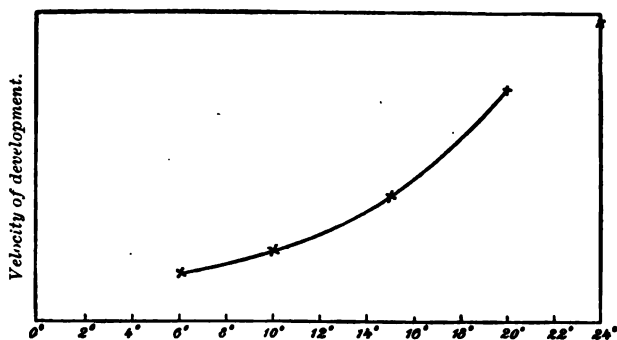


FIG. 10.

Hertwig measured the periods of time in which a given developmental stage was reached at various temperatures. These time intervals are inversely proportional to the rate of development.

Upon the ordinates of our curves are given the time intervals (days); upon the abscissas, the temperatures. The observations include the temperatures from 6° to 24°.

The curve in Fig. 10 is based upon the following table;

STAGE I IN DEVELOPMENT WAS REACHED:

	Velocity of Development.
At 6° in 4.75 days .....	1
" 10 " 3.16 " .....	1.2
" 15 " 2 " .....	2.4
" 20 " 1.2 " .....	3.9
" 24 " 1 " .....	4.75

If we consider the velocity at 6° as equal to 1, then at 10° it equals  $\frac{4.75}{3.16} \times 1 = 1.2$ ; at 15° it equals  $\frac{4.75}{2} \times 1 = 2.4$ ,

**TEMPERATURE AND REACTION VELOCITY. 63**

etc. The figures of the third column were obtained in this way.

**STAGE II IN DEVELOPMENT WAS REACHED:**

		Velocity of Development.
At 6° in 7	days	.....1
" 10 " 5	"	.....1.4
" 15 " 3	"	.....2.3
" 20 " 1.6	"	.....4.4
" 24 " 1.25	"	.....5.6

Such tables can be made for each of the different (7) stages investigated. The rate of development at 6° is taken in each instance as equal to 1. In this manner the following table is obtained:

Temper- ature.	I	II	III	IV	V	VI	VII	Aver- age.
6°	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0
10	1.2	1.4	1.4	1.5	1.6	1.6	1.8	1.5
15	2.4	2.3	2.25	2.4	2.8	3.0	3.5	2.6
20	3.9	4.4	4.5	4.6	5.3	5.5	6.0	(4.9)
24	4.95	5.6	6.0	6.0	7.0	7.0	7.5	(6.3)

The curve in Fig. 10 has been constructed from the figures of the last column. The fact that the values obtained in the horizontal rows (particularly those below 20°) show no great variations (where these exist they are to be attributed in part to variations in temperature) makes possible the calculation of an average without great error. Here also an increase in temperature of 10° doubles or trebles the velocity; in other words, a temperature effect as great as that in simple chemical reactions exists here too.

What Hertwig himself thinks of the continuation of these observations is shown most clearly in his own words: "I intend to examine the questions suggested here more accurately in experiments upon the eggs of echinoderms,



which I consider most suitable for such investigations, and shall then try to see in how far the whole subject is capable of strict mathematical treatment."

Of prime importance is the answer to the question, What influence has temperature upon the rapidity with which poisons (or medicines) show their effects? The great experimental difficulties that stand in the way of an exact investigation of this subject have not yet been overcome, for until recently none of the principles of physical chemistry have been employed.

For the first observations in this direction we are indebted to Alexander von Humboldt,\* for this old master of biology found that heat increased the activity of such substances as "oxygenierte Kochsalzsäure" (chlorine), opium, and alcohol, no less than the action of alkali sulphides. The experiments were in those days made upon the elementary tissues, heart, and motor nerves.

Kunde,† Hermann,‡ and Kronecker § also studied this question, and Cl. Bernard || found that while even the most intense poisons take effect very slowly upon cooled frogs, they act the more rapidly the higher the temperature.

The more recent investigations of Luchsinger, ¶ Brunton,\*\*

\* Über die gereizte Muskel- und Nervenfasern II, 218 (1797).

† Verhandlungen der physik.-medizin. Gesellschaft in Würzburg 1857, 175; Virchows Arch. 18, 357 (1860).

‡ Dubois-Reymonds Archiv für Anatomie und Physiologie 1867. 64.

§ Ibid. 1881, 357.

|| Leçons sur les anesthésiques et sur l'asphyxie, Paris 1875, 132.

¶ Physiolog. Studien. Thermisch-toxikologische Untersuchungen. Leipzig 1882.

\*\* Handbuch der allgem. Therapie und Pharmakologie, Leipzig 1893, 48.

Stokvis,\* and Saint Hilaire,† who worked upon this subject under Richet's direction, have only shown the difficulties that lie in the way of an answer to this question.

It is difficult to follow quantitatively the influence of temperature upon the velocity with which chemical agents act upon the animal organism because various factors play a rôle in bringing about the final result.

Thus the absorption velocity changes with changes in temperature, while the irritability of organisms and tissues is also dependent to a large extent upon the temperature.

The influence of temperature upon the velocity of intoxication as determined by our measurements is therefore the sum of the influence of temperature upon various life phenomena which can be analysed into their constituents only with the greatest difficulty.

While Richet ‡ is of the opinion that the variations in the reaction velocity at various temperatures between a tissue and a poison are determined solely by the temperature, Stokvis § has proved that the irritability of the tissue also plays a heavy rôle in the process.

For if at a low temperature the poison is increased in amount to correspond to the decreased *irritability* of the tissues brought about by lowering the temperature, the same velocity of intoxication may be attained under these circumstances as at higher temperatures.

Later we shall discuss in greater detail the bactericidal

\* Feestbundel voor Donders, Amsterdam 1888, 465.

† Thèse, Paris 1888.

‡ Bulletin de la Société de Biologie, 18. April 1895.

§ l. c.

powers of various disinfectants, but we will point out here that temperature has a great influence upon the velocity of disinfection also. Heider \* in particular has studied this question quantitatively, after observations had been made in the same direction by Koch,† Nocht,‡ Henle,§ and Pane.||

Heider, for example, found that anthrax spores which had not been destroyed after an exposure for thirty-six days to the action of a 5 per cent carbolic acid solution at room temperature, were killed after three minutes when the temperature was raised to 75°.¶

The practical value which a study of the influence of temperature upon the velocity of the action of various therapeutic agents might have manifests itself most clearly when we remember, for example, that the reactions which occur in a feverish organism take place much more rapidly than those in the normal individual, and that the same velocity is to be expected \*\* only when the increase in temperature is taken into consideration and the dose of medicine administered to the patient is diminished correspondingly.

\* Arch. f. Hyg. 15, 341 (1892).

† Über Desinfektion, Mitteilungen aus dem Kaiserlichen Gesundheitsamte I (1881).

‡ Zeitschr. f. Hyg. 7 (1889).

§ Arch. f. Hyg. 11, 188 (1889).

|| Atti della R. Accademia medica di Roma (2) 5 (1890).

¶ An especially arranged experiment had shown that a rise in temperature to 75° does not injure the bacteria if kept in pure water.

\*\* In what manner the effect of the drug is associated with this velocity is a question by itself, into a discussion of which we cannot enter here. See E. Juckuff, Versuche zur Auffindung eines Dosierungsgesetzes. Leipzig 1895

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An extensive field for investigation is therefore opened here, in which the physico-chemical principles discussed above can point the way.\*

\* See Stokvis, Atti dell' XI Congresso medico internazionale, Roma 1894, p. 354.

## FIFTH LECTURE.

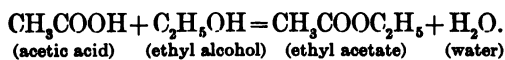
### Equilibrium.

WE have already pointed out (p. 3) that two classes of phenomena are governed by the law of mass action: first, reaction velocity; second, equilibrium, which is established when the reaction has come to an end.

In the discussion of the extensive field of the phenomena of equilibrium, we shall consider in detail especially those which, because of their direct or indirect bearing upon physiological or biological problems, demand our attention most particularly. For a better understanding of the subject, however, it may perhaps be necessary to deal first of all with a few of the more purely physico-chemical phenomena.

If a number of substances capable of reacting chemically with each other are brought together, a reaction ensues which after a given time comes to a standstill (practically),—the system is in chemical equilibrium. The rapidity with which this state of equilibrium is reached is dependent upon the velocity of the given reaction (consequently upon the temperature, and the medium in which the reaction occurs).

If, for example, we mix, at a definite temperature, equivalent amounts of acetic acid and ethyl alcohol, a reaction ensues according to the equation



The reaction takes place in the direction from left to right.

If, however, we bring equivalent amounts of ethyl acetate and water together, ethyl alcohol and acetic acid are formed,—in other words, the above reaction takes place from right to left.

Neither in the first nor in the second instance does the reaction become complete; before the given amounts of acetic acid and ethyl alcohol, or ester and water, have undergone complete decomposition the reaction ceases. A condition of equilibrium is established which may be represented, according to van't Hoff, by the following:



The system found to the left of the  $\rightleftharpoons$  sign we shall hereafter designate the *first*, that to the right the *second* system.

A reaction such as the above, which can take place from left to right, as well as from right to left, is called a *reversible* reaction.

As can further be seen from equation (1), after equilibrium has been established, the four substances reacting with one another are present in the reaction mixture. The characteristic feature of such a condition of equilibrium is found in the fact that it is always the same (we always assume in our considerations that the external conditions governing the reacting system, such as pressure and temperature, remain constant) no matter from which side it is reached. In other words, it is immaterial whether we mix one mol acetic acid with one mol ethyl alcohol, or one mol ethyl acetate with one mol water,—the condition of equilibrium reached in either case is entirely the same.

Now this behaviour is in no way an exception to what generally occurs in a reaction between different substances. On the contrary, the statement can be made that nearly all reactions are reversible.

We shall see later that under certain conditions equilibrium may lean particularly toward one side, that is to say, under certain conditions the first or the second system may be so prominent that the presence of the other system can no longer be recognised by the analytical means at our disposal. The given reaction then no longer gives the impression of a balanced action,\* but seems to have proceeded completely toward one side.

If, for example, we bring sulphuric acid ( $\text{H}_2\text{SO}_4$ ) and sodium hydroxide ( $\text{NaOH}$ ) together, an apparently complete transformation into sodium sulphate ( $\text{Na}_2\text{SO}_4$ ) and water ( $\text{H}_2\text{O}$ ) takes place, and the reverse process in which sodium sulphate is decomposed into sodium hydroxide and sulphuric acid by water seems not to occur. There are, nevertheless, a number of reasons at hand for assuming that the last-named process actually does occur, and that in consequence, at the end of the reaction, sulphuric acid, sodium hydroxide, sodium sulphate, and water are present in the reaction mixture. Only the amounts of sulphuric acid and sodium hydroxide present are so small that they cannot be proven to exist by the analytical means at our disposal. As the delicacy of our analytical reactions increases, the number of known balanced actions grows accordingly.

A consideration of the fact that the decomposition represented in equation (1) takes place because two reactions

\* Reactions that proceed to an equilibrium are also known as balanced actions.

occur simultaneously but in opposite directions, points the way for a sharp definition of the condition of equilibrium.

We shall choose as an example the formation of ethyl acetate from acetic acid and ethyl alcohol.

If we consider the reaction



it can be said that double decomposition between the acetic acid and the alcohol molecules can occur only where these molecules meet.

The number of such collisions between molecules in the unit time is clearly proportional to the concentration of the acid ( $C_{\text{acid}}$ ) and that of the alcohol ( $C_{\text{alc.}}$ ).

The velocity ( $s_1$ ) with which the reaction represented in equation (2) occurs is therefore

$$s_1 = k_1 C_{\text{acid}} \times C_{\text{alc.}}, \quad (3)$$

where  $k_1$  represents the velocity with which the reaction would take place if both of the reacting substances had the unit concentration.

Simultaneously with reaction (2) the following opposing reaction takes place:



If the concentration of the ester is  $C_{\text{ester}}$ , that of the water  $C_{\text{water}}$ , then the velocity of this decomposition ( $s_2$ ) is

$$s_2 = k_2 C_{\text{ester}} \times C_{\text{water}}, \quad (5)$$

wherein  $k_2$  is the velocity with which this reaction (4) would occur if both of the reacting substances had the unit of concentration.

When equilibrium has been reached, then

$$s_1 = s_2;$$

consequently, according to (3) and (4),

$$k_1 C_{\text{acid}} \times C_{\text{alc.}} = k_2 C_{\text{ester}} \times C_{\text{water}},$$

or

$$\frac{k_1}{k_2} = \frac{C_{\text{ester}} \times C_{\text{water}}}{C_{\text{acid}} \times C_{\text{alc.}}} \quad (6)$$



The relation  $\left(\frac{k_1}{k_2}\right)$  between the velocity constants of the two opposed reactions is known as the *equilibrium constant* ( $K$ ) of the reaction. Therefore

$$K = \frac{k_1}{k_2} = \frac{C_{\text{ester}} \times C_{\text{water}}}{C_{\text{acid}} \times C_{\text{alc.}}} \quad (7)$$

We see from this equation that when equilibrium has been established, a definite relation ( $K$ ) exists between the product of the concentrations of the reacting substances, ester and water upon the one hand, and acid and alcohol upon the other.

If molecular amounts of the acid and the alcohol are brought together, experiment shows that equilibrium is established as soon as two thirds of the amount of the substances present has undergone decomposition. If we designate the original concentration of the acid by  $C$  (the concentration of the alcohol is then also equal to  $C$ ), then for the example given here

$$K = \frac{\frac{2}{3}C \times \frac{2}{3}C}{\frac{1}{3}C \times \frac{1}{3}C} = 4. \quad (8)$$

From this value of  $K$  we can now predict at what point equilibrium will be established when we bring together any given amounts of acid and alcohol, for the relation expressed by equation (8) must always exist, in the state of equilibrium, between the concentrations of the substances present.

For example, let us ask the question: When one molecule of acetic acid is mixed with  $a$  molecules of alcohol, how many molecules of the acid will have been decomposed when equilibrium has been established?

If we let  $\gamma$  equal this number, then, since originally one molecule of acetic acid was present, in equilibrium

$$\begin{array}{llll} \text{the concentration of the acetic acid, } C_{\text{acid}} & = & 1 - \gamma, & \\ \text{“ “ “ “ alcohol, } C_{\text{alc}} & = & a - \gamma, & \\ \text{“ “ “ “ ester, } C_{\text{ester}} & = & \gamma, & \\ \text{“ “ “ “ water, } C_{\text{water}} & = & \gamma. & \end{array}$$

Then, according to equation (8),

$$K = 4 = \frac{\gamma \times \gamma}{(1 - \gamma)(a - \gamma)}$$

Developing this equation and finding the value of  $\gamma$  gives

$$\gamma = \frac{1}{2}(a + 1 - \sqrt{a^2 - a + 1}).$$

Berthelot and Péan de St. Gilles,\* to test the correctness of this equation, mixed one molecule of acetic acid with various amounts ( $a$  molecules) of alcohol, and after establishment of equilibrium determined experimentally the value of  $\gamma$ , which was at the same time calculated by the above equation.

The following table shows how well the calculated values agree with those determined experimentally:

$a$	$\gamma$ (observed).	$\gamma$ (calculated).
0.05	0.05	0.049
0.08	0.078	0.078
0.18	0.171	0.171
0.98	0.226	0.232
1	0.665	0.667
8	0.966	0.945

The table shows that when, for example, one molecule of acetic acid is mixed with 8 ( $a=8$ ) molecules of alcohol, equilibrium will be established when 0.966 molecules of the

\* *Annales de chimie et de physique* 65, 385 (1862); 66, 5 (1862); 68, 225 (1863). See also van't Hoff, *Ber. d. deutsch. chem. Gesellsch.* 10, 669 (1870).

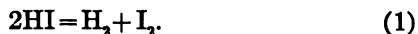
acid, that is 96.6 per cent, have been changed to ethyl acetate.

The fact is yet to be emphasised that the rapidity with which equilibrium is established increases with an increase in temperature. Equilibrium *in this particular case* is, however, almost independent of temperature, that is to say, the concentrations of the substances present in the reaction mixture after the establishment of equilibrium are independent of the temperature. In the given instance, therefore, where one molecule of acetic acid reacts with 8 molecules of alcohol we cannot, through an increase in temperature, bring about the decomposition of more than 96.6 per cent of the acid.\*

In the formation of an ester from acid and alcohol we are dealing with an equilibrium in a *homogeneous liquid* system. All the substances present, acid, alcohol, ester, and water, are homogeneously mixed.

We shall now direct our attention to a system which is also homogeneous, though not liquid, but gaseous.

If hydriodic acid (HI) is heated in a closed chamber, it is decomposed into its constituents according to the formula



Such a process is termed *dissociation*. The hydriodic acid *dissociates* into hydrogen and iodine. Such phenomena were first studied by Georges Aimé in 1837, and very thoroughly by Sainte Claire Deville in 1857.

If the temperature is kept constant, the pressure does not vary during this operation. Our equation states that

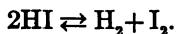
\* The reason why temperature has no influence upon the state of equilibrium in this particular case will be discussed later.

two volumes of hydriodic acid yield one volume of hydrogen and one volume of iodine vapor. The total volume consequently remains unaltered during the decomposition, and therefore the pressure remains unaltered also.

But hydrogen and iodine can also combine, according to the equation



In accordance with the facts given on p. 68, it can be easily seen that the two simultaneously occurring reactions (1) and (2) must lead to the establishment of an equilibrium, which may be represented by the equation



What relation now will exist between the concentrations of the reacting substances in the state of equilibrium?

The velocity ( $s_1$ ) with which the reaction

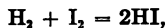


takes place may be represented, according to Guldberg and Waage, by the equation

$$s_1 = k_1 C_{\text{HI}} \times C_{\text{HI}} \quad (4)$$

Herein  $C_{\text{HI}}$  represents the concentration of the hydriodic acid, while  $k_1$  is the velocity with which the reaction would proceed if the concentration of the hydriodic acid were equal to 1.

In a similar manner the velocity with which the reconstruction of the hydriodic acid out of its constituents occurs, that is the velocity of the reaction,



may be represented by the equation

$$s_2 = k_2 C_{\text{H}_2} \times C_{\text{I}_2} \quad (5)$$

When equilibrium is established, then

$$s_1 = s_2.$$

Wherefore  $k_1 C_{\text{HI}} \times C_{\text{HI}} = k_2 C_{\text{H}_2} \times C_{\text{I}_2},$

or  $k_1 C_{\text{HI}}^2 = k_2 C_{\text{H}_2} \times C_{\text{I}_2},$

$$\frac{k_2}{k_1} = K = \frac{C_{\text{HI}}^2}{C_{\text{H}_2} \times C_{\text{I}_2}}, \quad (6)$$

or in words: The equilibrium constant ( $K$ ), which we shall here call the *dissociation constant*, is equal to the square of the concentration of the undissociated hydriodic acid, divided by the product of the concentration of the hydrogen and iodine vapour.

Equation (6) may be stated in a different form if one remembers that the concentration of a gas (the number of mols per litre) is proportional to the pressure of the gas. For we are able, by increasing the pressure upon a given weight of gas, for instance doubling it, to bring into the same volume twice the number of molecules of the gas.

If we represent the pressure of the hydriodic acid (that is, the partial pressure exerted by the undissociated hydriodic acid in the gas mixture  $\text{HI} + \text{H}_2 + \text{I}_2$ ) as equal to  $p_{\text{HI}}$ , the partial pressures of hydrogen and iodine vapour as equal to  $p_{\text{H}_2}$  and  $p_{\text{I}_2}$ , equation (6) assumes the following form:

$$K = \frac{p_{\text{HI}}^2}{p_{\text{H}_2} \times p_{\text{I}_2}}, \quad (7)$$

or in words: When equilibrium is established, the square of the partial pressure of the hydriodic acid divided by the product of the partial pressures of the hydrogen and iodine vapour is a constant. By means of this equation the question can now be immediately answered: What will happen if, at constant temperature, the pressure under which the gas mixture ( $\text{HI} + \text{H}_2 + \text{I}_2$ ) exists is increased?

Will the dissociation of the hydriodic acid increase, decrease, or remain unaltered?

If we compress the gas mixture to the  $n$ th part, that is to say, if we decrease its volume  $n$  times, then according to the law of Boyle, which states that at constant temperature the pressure of a given weight of gas is inversely proportional to the volume, the pressure will be increased  $n$  times.

Consequently  $p_{\text{HI}}^2$  becomes  $n^2 \cdot p_{\text{HI}}^2$ ,  $p_{\text{H}_2}$  becomes  $np_{\text{H}_2}$ , and  $p_{\text{I}_2}$  becomes  $np_{\text{I}_2}$ ; and the equilibrium constant becomes

$$\frac{n^2 p_{\text{HI}}^2}{np_{\text{H}_2} \times np_{\text{I}_2}} = \frac{p_{\text{HI}}^2}{p_{\text{H}_2} \times p_{\text{I}_2}} = K,$$

which is to say that the state of equilibrium is independent of the pressure exerted upon the system in which the equilibrium is established.

This is a sequel to the fact that the volume is not altered by the dissociation, for two volumes of HI yield one volume of  $\text{H}_2$  and one of  $\text{I}_2$ .

Bodenstein \* in particular has exhaustively studied the dissociation of hydriodic acid quantitatively, and has proved the correctness of equation (7).

Equally interesting is the question: What will happen when we add to the gas mixture after equilibrium has been established any indifferent gas, such as nitrogen, while the volume of the mixture is left unchanged? Will the dissociation change in this case? It is evident from the beginning that the dissociation will undergo no change. According to the law of Dalton, when different gases are

\* Zeitschr. f. physik. Chem. 12, 392 (1893); 13, 56 (1894); 22, 1 (1897). See also Lemoine, Etudes sur les Equilibres chimiques, p. 72, Paris 1881. Extrait de l'Encyclopédie chimique dirigée par M. Frémy.

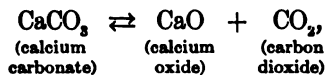
mixed in a container, the partial pressure of each gas is not changed by the presence of the others.

If, therefore, we add to the gas mixture of hydriodic acid, hydrogen, and iodine vapour (without changing its volume) any given amount of nitrogen, the partial pressures  $p_{\text{HI}}$ ,  $p_{\text{H}_2}$ , and  $p_{\text{I}_2}$  remain unaltered, and since equilibrium is dependent upon these values (see equation 7), it, also, will not change.

The case is, however, entirely different if (at constant volume) we add a certain amount of one of the dissociation products (hydrogen or iodine vapour) to the gas mixture. If, for example, we introduce hydrogen into the mixture, the partial pressure  $p_{\text{H}_2}$  is increased, and since  $K$  must remain constant,  $p_{\text{HI}}^2$  will increase. The same would be the case if any given amount of iodine vapour were added to the gas mixtures:  $p_{\text{I}_2}$  would then increase, and also  $p_{\text{HI}}^2$  to a corresponding degree. We can consequently draw the following conclusion: *Dissociation is decreased through the addition of the products of dissociation.*

Of great practical importance is the dissociation which calcium carbonate ( $\text{CaCO}_3$ ) suffers in the so-called process of *burning*.

In this case a solid substance ( $\text{CaCO}_3$ ) yields upon dissociation a different solid substance, calcium oxide ( $\text{CaO}$ ) and a gas, carbon dioxide ( $\text{CO}_2$ ). The system resulting from this reaction, which takes place according to the formula



is a *heterogeneous* one.

which is to say: *When calcium carbonate dissociates into calcium oxide and carbon dioxide, the pressure of the carbon dioxide has at constant temperature a constant value, independent of the proportions in which the solid substances are present.*

This tension of the carbon dioxide is designated the *dissociation tension* of the calcium carbonate at the given temperature.

So, for example, Le Chatelier found:

Temperature.	Dissociation tension of the calcium carbonate in mm. of mercury.	Temperature.	Dissociation tension of the calcium carbonate in mm. of mercury.
547°	27	745	289
610	46	810	678
625	56	812	763
740	255	865	1333

We see from the table that when, for example, at 625° any given amount of calcium carbonate is introduced into a closed vessel, CaO and CO<sub>2</sub> will be formed until the tension of the carbon dioxide becomes 56 mm. Equilibrium is then established, and the system undergoes no further change.

If at this temperature the pressure of the carbon dioxide is increased, the carbon dioxide and the CaO will be reconverted into CaCO<sub>3</sub>, and this process will continue until the pressure of the carbon dioxide has again fallen to 56 mm.

If the tension of the carbon dioxide is decreased by removing a certain amount of this gas from the mixture, then, through the decomposition of a fresh quantity of the carbonate, CaO and CO<sub>2</sub> will be formed until the dissociation tension of 56 mm. is again reached.



## SIXTH LECTURE.

### Equilibrium (Continued).

WE shall now consider in the light of the law of mass action a few facts from our knowledge of respiration.

If blood is exhausted under the receiver of an air-pump, three gases are liberated: oxygen, carbon dioxide, and nitrogen. In how far the last-named gas plays a rôle in the respiratory process seems not yet to be entirely established.

Upon the other hand, the presence of the oxygen and the carbon dioxide is of physiological importance.

The arterial blood of the dog, upon which most analyses have been made, holds 19-25 volumes of oxygen in each 100 volumes of blood, as calculated at 0° and 760 mm. of mercury pressure.

This large amount of oxygen cannot be held in the blood in simple solution, for 100 volumes of water absorb only about 4.8 volumes of gas at 0° from a pure oxygen atmosphere at 760 mm. pressure; according to the law of Henry, which states that the amount of a gas absorbed by a definite volume of a liquid is proportional to the pressure of the gas, 100 volumes of water can therefore absorb only about 1 volume of oxygen from ordinary air, in which the oxygen has a pressure of only one fifth of an atmosphere.

Furthermore, since the temperature of the body is 37°, and since gas absorption diminishes with an increase in temperature, the water of the blood could at this temperature absorb only less than 1 volume of oxygen. Besides this,

gases dissolve with greater difficulty in concentrated solutions than in pure water; for this reason also, since blood is to be regarded as a fairly concentrated aqueous solution of various substances, the value 1 will have to be still further diminished.

If now it is found that in 100 volumes of blood 19-25 volumes of oxygen are absorbed, another factor must be concerned in bringing about this result.

Now we know that the hæmoglobin present in the blood is the substance which makes possible the high oxygen content of the blood.

If hæmoglobin is brought together with oxygen, oxyhæmoglobin is formed. The chemical composition of hæmoglobin as well as that of oxyhæmoglobin is entirely unknown.

Hæmoglobin can also take up oxygen when in aqueous solution and so furnish an aqueous solution of oxyhæmoglobin.

Since Donders \* in 1872 first showed that the taking up of oxygen by hæmoglobin is a reversible process, and that it could be put into the category of the phenomena of dissociation known at that time, this process has been much studied by many physiologists.

The decomposition that occurs here may be represented by the following equation:



Hüfner † has gone deeply into the study of the problem: What quantitative relations exist between the pressure of

\* Pflügers Arch. 5, 20 (1872).

† Dubois-Reymonds Archiv, Physiol. Abt. 1 (1890). Zeitschr. f. physiol. Chem. 10, 218 (1886); 12, 568 (1888); 13, 285 (1889).

the oxygen found above an aqueous solution of oxyhæmoglobin and the composition of this solution ?

Especially arranged experiments had shown that blood and aqueous solutions containing the same amount of hæmoglobin show the same behaviour toward oxygen; this fact justified Hüfner in making his further experiments with aqueous solutions of hæmoglobin instead of blood. In most text-books of physiology great stress is laid upon the analogy that is supposed to exist between the dissociation of the oxyhæmoglobin of the blood, into hæmoglobin and oxygen, and the dissociation of calcium carbonate into calcium oxide and carbon dioxide. This analogy is, however, only an apparent one, for in the case of the oxyhæmoglobin in the blood we are dealing with a more complicated process. If we examine the condition of affairs a little more closely, we see that the dissociation of calcium carbonate goes on in a heterogeneous system. When oxyhæmoglobin dissociates in aqueous solution, we are dealing with two states of equilibrium,—first, with the homogeneous equilibrium between oxyhæmoglobin (dissolved in water), hæmoglobin (dissolved in water), and oxygen (dissolved in water); secondly, with the heterogeneous equilibrium between the oxygen dissolved in the water and the gaseous oxygen above the water.

The analogy referred to would exist only if we were dealing with the dissociation of solid oxyhæmoglobin into solid hæmoglobin and oxygen, but the presence of such a state of equilibrium in the blood is out of the question.

Later we shall learn of a second reason which shows how insufficient the advancement of such an analogy is.

Hüfner determined in his investigations the pressure of oxygen that is in equilibrium, at a definite temperature,

with oxyhæmoglobin solutions of known composition. For this purpose the given solution is shaken at a constant temperature with pure nitrogen. Because of the dissociation tension of the oxyhæmoglobin, oxygen is liberated, the pressure of which may be measured with a manometer.

The law of Dalton underlies this measurement, according to which the presence of the nitrogen has no influence upon the oxygen pressure.

We shall now consider somewhat more closely the experiments made by Hufner at 35°, since this temperature is approximately that of the body, and these measurements are in consequence of the greatest interest from a physiological standpoint.

If, in the state of equilibrium (in aqueous solution)



the concentration of the oxyhæmoglobin is  $C_o$ , that of the hæmoglobin  $C_H$ , that of the oxygen  $C_s$ , then, according to the law of mass action,

$$k_1 C_o = k_2 C_H \times C_s. \quad (1)$$

Herein  $k_1$  is the velocity with which, at the temperature of the experiment, the oxyhæmoglobin dissociates into its components;  $k_2$  that with which, under the same conditions, it is re-formed from its components.

$C_o$  is the concentration of the oxyhæmoglobin when equilibrium has been established; similarly  $C_H$  is the concentration of the hæmoglobin under the same conditions.  $C_s$ , now, is not the concentration of the oxygen which has been liberated in consequence of the dissociation of the oxyhæmoglobin, but only that portion of the gas which,

under the existing conditions of temperature and pressure, is still present in the solution. It is to be remembered that the existing equilibrium prevails between the oxygen and the hæmoglobin in the solution.

Now  $C_s$ , according to the law of Henry, with which we shall become acquainted immediately, is proportional to the pressure of the oxygen. We may therefore write  $C_s = Fp$ , wherein  $F$  is a numerical factor, and  $p$  is the oxygen pressure.

Our equation (1) then becomes

$$k_1 C_o = k_2 C_H F p.$$

Since  $F$  is a constant, we can call  $k_2 F = \text{constant} = k_3$ , wherefore

$$k_1 C_o = k_3 C_H p,$$

or

$$\frac{k_3}{k_1} = \frac{1}{K} = \frac{C_o}{C_H \times p}. \quad (2)$$

If now the dissociation constant  $K$  is known, then we can calculate (see p. 72) how many per cent of the oxyhæmoglobin are dissociated at the given oxygen pressure.

Hüfner uses this equation (1) as his starting-point, and bases his further deductions upon it. It is to be noted that equation (1) assumes that oxyhæmoglobin is composed of one molecule of hæmoglobin and one molecule of oxygen. Should this not be the case,—and we can say nothing definite concerning this question at present,—equation (1) (and likewise equation (2)), as well as the conclusions drawn therefrom, would assume a somewhat

different form, corresponding to the change in the number of molecules.

To this is to be added the fact that Hüfner in his calculations has considered the amount of oxygen taken up (at 35°) by solutions of hæmoglobin, which contain up to 25 per cent solid matter, equal to that absorbed by pure water at the same temperature, while, as is known, the absorption capacity of liquids decreases with an increase in the amount of substance dissolved therein.

Hüfner's experiments showed that in the dissociation of oxyhæmoglobin the oxygen pressure is, *ceteris paribus*, dependent upon the amount of oxyhæmoglobin dissociated. If we accept this result as correct, as probably most textbooks of physiology do, there is certainly no reason (as even Hüfner himself emphasises) for discovering in this dissociation process an analogue of the dissociation of calcium carbonate. For one finds, *ceteris paribus*, in the dissociation of calcium carbonate at constant temperature a definite pressure of carbon dioxide, independent of the amount of dissociated substance.

The change that hæmoglobin suffers when brought together with carbon monoxide has also been thoroughly studied by Hüfner; \* here also, under the assumption that the reaction takes place between one molecule of each of the substances, he finds that the pressure of the dissociated gas maintains a value which is dependent upon the concentration of the undissociated carbonic oxide hæmoglobin. We can therefore not regard this dissociation as an analogue of the dissociation of calcium carbonate either.

\* Dubois-Reymonds Archiv, Physiol. Abt. 1895, 213. Extensive references to the literature may be found in W. Sachs: Die Kohlenoxydvergiftung. Braunschweig 1900.

Bunge \* in his text-book of physiological chemistry asks, "How can the mere vacuum dissociate the oxyhæmoglobin?" and answers, "In reality it is not the vacuum that dissociates the oxyhæmoglobin, but heat. At very low temperature—under  $0^{\circ}$ —an oxyhæmoglobin solution may be permitted to evaporate to dryness without decomposition occurring in the precipitated crystals of oxyhæmoglobin." But this explanation of the process cannot be correct.

This dissociation, the splitting off of oxygen, will indeed take place only very slowly and but to a slight degree, since the temperature is low and the reaction velocity and the dissociation tension is in consequence slight; but since the oxyhæmoglobin has at every temperature, no matter how low, a definite dissociation pressure (which disappears only at absolute zero, that is, therefore, at  $-273^{\circ}$  C.) and the external pressure of oxygen in vacuo is zero, the dissociation will always occur. It is of course possible that it may be so slight as to evade actual detection when the experiment is not continued for a very long time.

#### SOLUBILITY.

The phenomena of solubility form a very important group of states of equilibrium. Inasmuch as we are acquainted with three states of aggregation, there are also three different kinds of solutions, namely, gaseous, liquid, and solid.

\* *Lehrb. d. physiol. Chem.*, Leipzig 1898, p. 260. See also Landois, *Lehrb. d. physiologie des Menschen*, p. 70. 10 Ed. Berlin and Vienna 1900.

We must therefore distinguish between the following varieties of solutions:

1. Solutions of gases in gases (gaseous).
2. Solutions of gases in liquids (liquid).
3. Solutions of gases in solids (solid).
4. Solutions of liquids in liquids (liquid).
5. Solutions of solids in liquids (liquid).
6. Solutions of solids in solids (solid).

Of these varieties those given under 2 and 5 are for our purposes the most important; yet we shall also touch upon group 6, though only very briefly.

#### SOLUTIONS OF GASES IN LIQUIDS.

If at constant temperature and under constant pressure a liquid (for example, water) is shaken together with a gas (for example, carbon dioxide) which is soluble in it, no more of the gas will after a certain time be taken up by the liquid,—equilibrium will have been established. This equilibrium is governed by the law of Henry.

This law may be expressed as follows: The weight of a gas dissolved by a given amount of liquid is, at constant temperature, proportional to the pressure of the gas; or also: A given amount of liquid dissolves at constant temperature always the same volume of a given gas, independently of the pressure of the gas.

If, therefore, a certain amount of water dissolves at a given temperature 1 g. of carbon dioxide under 1 atmosphere of pressure, then the same amount of water will dissolve 2 g. of carbon dioxide of 2 atmospheres pressure; for these 2 g. of carbon dioxide have at 2 atmospheres pressure the same volume as 1 g. at a pressure of 1 atmosphere.



If we are dealing with the solution of a mixture of different gases in a liquid, the law of Dalton holds, which states: When a mixture of gases goes into solution in a liquid, each component is dissolved in proportion to its partial pressure. This law may also be stated in the following form: When a mixture of gases goes into solution in a liquid each gas is dissolved as though the other gases were absent.

Yet it must be remembered that the law of Henry and the law of Dalton hold strictly only when the gas is but slightly soluble and its pressure does not exceed a few atmospheres.

The *absorption coefficient* of a gas in a liquid is, according to Bunsen, the volume of this gas, reduced to 0° and 760 mm. of mercury pressure, which 1 c.c. of this liquid absorbs if the pressure of the gas is 760 mm.

If, for example, it is found that  $V$  volumes of a liquid absorb  $v$  volumes of a gas at the temperature  $t^\circ$  and a pressure of  $p$ , Bunsen reduces the known gas volume  $v$  to 0° and 760 mm.

Now the volume  $v$ , measured at the temperature  $t^\circ$  and the pressure  $p$  mm., is at 0° and the pressure  $p$  mm. equal to  $\frac{v}{1 + \alpha t}$  when  $\alpha$  represents the expansion coefficient ( $= \frac{1}{273}$ ) of gases.

The volume  $\frac{v}{1 + \alpha t}$ , measured at  $p$  mm., assumes at 760 mm. the volume

$$\frac{p}{760} \cdot \frac{v}{1 + \alpha t}$$

This volume was absorbed by the volume of liquid  $V$  at  $p$  mm. pressure; at a pressure of 760 mm., therefore, according to the law of Henry, a volume  $\frac{760}{p}$  as great will be absorbed, that is, therefore,

$$\frac{760}{p} \times \frac{p}{760} \times \frac{v}{1 + \alpha t} = \frac{v}{1 + \alpha t}$$

Consequently 1 c.c. of the liquid absorbs

$$\frac{1}{V} \frac{v}{1 + \alpha t} = \frac{v}{V(1 + \alpha t)} \text{ c.c. of the gas.}$$

This value represents the *Bunsen absorption coefficient*  $\beta$ .

$$\text{Wherefore} \quad \beta_{\text{Bunsen}} = \frac{v}{V(1 + \alpha t)}. \quad (1)$$

More recently, at Ostwald's suggestion, another value is often used, known as the *solubility* of a gas.

The solubility at  $t^\circ$  is the volume of a gas that is dissolved at this temperature by the unit volume (1 c.c.) of the given liquid.

If, for example, at  $t^\circ$  a volume of  $v$  c.c. of the gas is absorbed by  $V$  c.c. of the liquid, then the solubility at this temperature is

$$\lambda_{\text{Ostwald}} = \frac{v}{V}. \quad (2)$$

From equations (1) and (2),

$$\lambda_{\text{Ostwald}} : \beta_{\text{Bunsen}} = \frac{v}{V} : \frac{v}{V} \frac{1}{(1 + \alpha t)} = 1 : \frac{1}{(1 + \alpha t)},$$

$$\lambda_{\text{Ostwald}} = \beta_{\text{Bunsen}} (1 + \alpha t).$$

If the solubility of a gas, for example that of carbon dioxide, is to be determined, we have to determine experimentally the values  $v$  and  $V$  in equation (2).

It is to be remembered in this connection that the solubility of gases is a function of the temperature; with an increase in the temperature the solubility is diminished.

The apparatus which is at present much employed in such determinations has been patterned by Ostwald after an apparatus of Heidenhain and Meyer (see Fig. 11).

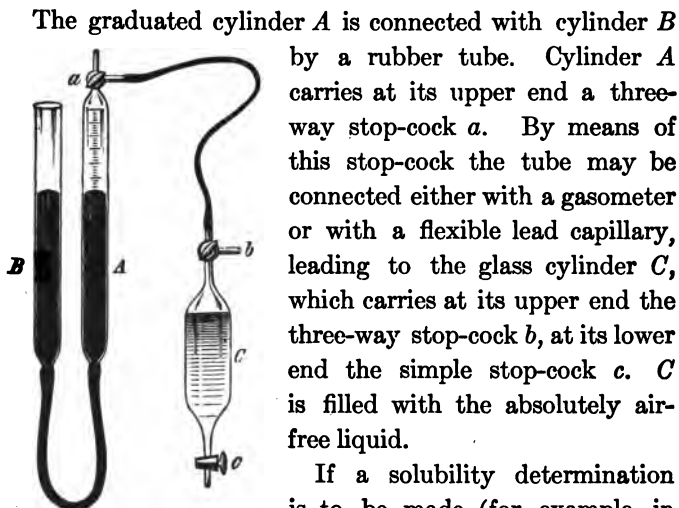


FIG. 11.

If a solubility determination is to be made (for example, in water), *A* and *B* are filled with mercury; by turning the stop-cocks *a* and *b* in the proper directions, the air can be driven out of the capillary. *a* is then opened in such a way that *C* is closed, and *b* is opened so that the tube *A* is connected with the gasometer. When the gas has been led into tube *A* (a drop of water is previously put into *A* so that the gas may become saturated with aqueous vapour), *a* is closed, and the volume of the gas, the temperature, and the height of the barometer are noted. *A* is then connected with the absorption vessel *C*; now as *B* is elevated and the stop-cocks *a* and *b* are opened, the gas moves into *C*, while a corresponding volume of water escapes from *C* which is collected in a tared flask and weighed. The gas now found in *C* is then shaken up at constant temperature with the water present therein until the volume in *A* no longer undergoes any change; the absorption is then at an end.

The volume of the gas in tube *A* is again noted, as is also the temperature and the height of the barometer, after which one has the necessary data for calculating the solubility.

If we assume that the temperature and the barometer have remained constant during the experiment, and also that *A* and *C* have always had the same temperature, our calculations will be as follows:

Suppose that *V* is the volume of the absorption vessel *C*, *V*<sub>0</sub> the amount of water that flowed out, *v*<sub>1</sub> the volume of the gas in the graduated tube *A* at the beginning of the experiment, *v*<sub>2</sub> its volume at the end of the experiment.

The volume of gas absorbed is then

$$v_1 - v_2 + V_0,$$

and the volume of the liquid that has absorbed this volume of gas

$$V - V_0.$$

The solubility at the given temperature is therefore

$$\lambda = \frac{v_1 - v_2 + V_0}{V - V_0}.$$

To obtain the gas-free liquid with which the vessel *C* is entirely filled at the beginning of the experiment, we use the apparatus of Ostwald represented in Fig. 12.

*K* is a so-called fractional distillation-flask, which is half-filled with the given liquid.

This flask is connected with a return condenser; the rubber tube used in the connection can be closed by means of a pinch-cock. While the liquid is heated the condensing tube and the flask are exhausted by an hydraulic air-pump. Boiling is continued until, upon shaking the bottle, the metallic rattle is heard which every liquid gives forth when entirely free from gas.

The pinch-cock is then closed, the condenser is removed, and *K* is connected with the absorption vessel of Fig. 11, which has previously been exhausted of air. By shaking and heating *K*, after the pinch-cock has been opened, the

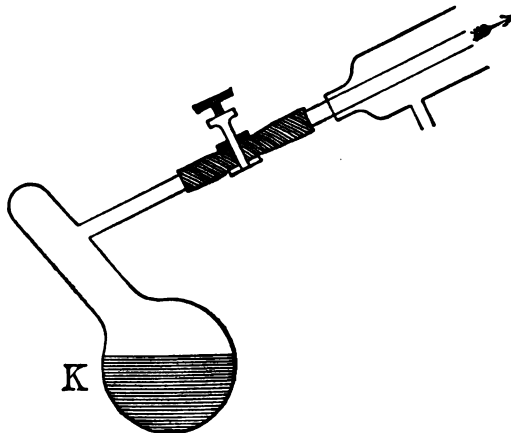


FIG. 12.

liquid is made to pass into *C*, and this vessel is closed as soon as it is entirely filled.

A large number of absorption coefficients were determined by Bunsen.\* Yet it must be remembered that the data obtained then have in recent years been greatly improved.

It has been found, in general, that gases are less soluble in concentrated salt solutions, *ceteris paribus*, than in pure water. Practical advantage is taken of this property of gases in storing them in gasometers.

Salt solutions (such as sodium chloride solutions) are used

\* Bunsen, *Gasometrische Methoden*, Braunschweig 1877

as pneumatic seals, since in this way the larger loss that would result from the absorption of the gas by pure water can be avoided.

From a physiological standpoint the observation of Setschenow is interesting, that at 15° C. the solubility of carbon dioxide in a 0.6 per cent sodium chloride solution (often called a physiological salt solution \*) is greater than that in pure water at the same temperature. This fact seems to indicate that carbon dioxide suffers some change when in dilute solution with sodium chloride.† Although from Setschenow's experiments the conclusion is to be drawn that the same relation exists also at 37° C. (body temperature), no direct experiments in this direction have yet been performed.

The following table contains a few data upon the solubility of different gases in water and salt solutions, which have been taken from the more recent determinations of Timofejew ‡ and Gordon.§

## ABSORPTION IN WATER.

Temperature.	HYDROGEN.	
	$\beta$	$\lambda$
0°	0.02153	0.02140
15	0.01903	0.01872
	OXYGEN.	
6.4	0.041408	.....
12.6	0.036011	.....

\* We shall return later to the so-called physiological salt solution.

† See Schultz, Pflügers Archiv 27, 454 (1882).

‡ Zeitschr. f. physik. Chem. 6, 141 (1890). See also L. W. Winkler, Berichte d. deutsch. chem. Gesellsch. 22, 1764 (1889); 24, 89 and 3602 (1893); 34, 1408 (1891). G. Just, Zeitschr. f. physik. Chem. 37, 342 (1901).

§ Zeitschr. f. physik. Chem. 18, 1 (1895).

## NITROGEN MONOXIDE (laughing gas).

Temperature.	In water.	In 12.182 per cent NaCl solution.
	$\beta$	$\beta$
5°	1.0955	0.63402
10	0.920	0.53227
15	0.7787	0.44947
20	0.670	0.38561

While, therefore, at 0° one litre of water absorbs 0.0214 litre of hydrogen, at 15° one litre of water takes up only 0.01872 litre of hydrogen; a distinct diminution in solubility therefore occurs with an increase in temperature.

## SEVENTH LECTURE.

### Equilibrium (Continued).

#### SOLUTIONS OF SOLIDS IN LIQUIDS.

If at constant temperature a solid is immersed in a liquid, then, for a certain period, a progressively increasing amount of solid goes into solution. Finally, however, the liquid will take up no more; equilibrium has been established between the solid substance and the resulting solution,—at the given temperature the solution is *saturated* with the solid.

In daily life, perhaps, these phenomena attain the greatest interest when we deal with the solution of salts in water. We shall therefore devote our further considerations particularly to this field. Equilibrium between the solid substance and the solvent will be reached most rapidly when a large amount of the former, in a finely pulverised state (that is, therefore, with a large surface) is brought together with a small amount of the liquid, and provision is made through shaking that the surfaces coming in contact with the liquid are constantly renewed.\*

The *solubility* of a substance in water at the temperature  $t^{\circ}$  is the amount of this substance (in grams) which dis-

\* For the saturation velocity in such cases see: Noyes and Whitney, *Zeitschr. f. physik. Chem.* 23, 689 (1897); Bruner and Toloczko, *ibid.* 35, 283 (1901); *Zeitschr. für anorganische Chemie* 28, 314 (1901); Drucker, *Zeitschr. f. physik. Chem.* 36, 173, 693 (1901); *Zeitschr. für anorganische Chemie* 29, 459 (1902).



solves in 100 g. of water. Yet it must be remembered that many authors define the solubility of a substance at  $t^\circ$  as the amount (in grams) of this substance present in 100 g. of the solution when saturated at this temperature.

We shall in what follows make use of the first definition, even though the second often offers many advantages.

If, for example, we find stated that at  $t^\circ$  the solubility in water of any given salt is  $L$  according to the second definition (that is to say, therefore, that at  $t^\circ$   $L$  grams of salt are present in 100 grams of the saturated solution), then we can calculate from it the solubility according to the first definition. In the 100 grams of saturated solution there are present, beside the  $L$  grams of salt,  $100-L$  grams of water; according to this, in 100 grams of water  $\frac{100}{100-L} \times L$  grams of salt are dissolved.

If, according to the first definition, the solubility is given as equal to  $L_1$ , and we wish to calculate therefrom how many grams of the salt are present in 100 grams of saturated solution, it need only be remembered that 100 grams of water with  $L_1$  grams of salt dissolved in them form  $100 + L_1$  grams of saturated solution. In 100 grams of this solution there are therefore present  $\frac{100}{100 + L_1} \times L_1$  grams of salt.

In general, the statement may be made that every solid is soluble in every liquid, in other words, that there are no solids which are "insoluble." When, in spite of this fact, the expression is frequently used that a substance is insoluble, then by it is to be understood that the substance under discussion is only *very slightly soluble* in the given solvent.

We shall see later, in dealing with the origin of electromotive forces, that there are many reasons at hand for assuming that even metals (even though only very slightly) are soluble in water.

To determine the solubility of a solid in a liquid is by no means a simple operation; only within the last few

years has it been realised that hours and days of shaking or stirring at constant temperature of an excess of the finely divided substance with the liquid is necessary to establish equilibrium (saturation). Neglect of the necessary precautions in these respects is responsible for the fact that different observers have found very diverse numerical values for the solubility of the same salt, at the same temperature, in the same solvent (see the following table). The enormous material that has accumulated in the literature of this subject previous to 1885 is, with few exceptions, to be regarded as entirely worthless. Even after this time we still find many doubtful data.

## SOLUBILITY OF SODIUM CHLORIDE IN WATER.

Temperature.	Solubility.	Observer.
25°	35.6	Kopp
25	35.8	"
25	36.13	Poggiale
25	35.81	Möller
25	35.90	Andreae

## SOLUBILITY OF CADMIUM SULPHATE IN WATER.

Temperature.	Solubility.	Observer.
0°	55.52	Etard
0	75.47	Mylius and Funk
0	75.52	Cohen and Kohnstamm

The variations amount to 30 per cent.

Solubility determinations of solids in liquids may be made by two different methods:

1. The liquid (for example, water) is shaken for a long time at constant temperature with an excess of the given substance (for example, salt). The resulting saturated solution is then separated from the sediment by filtration, and the amount of the substance that has gone into solution is determined by analysis.

2. Accurately weighed amounts of the solid and the liquid are put into a flask (or tube) and after sealing the flask they are shaken at different constant temperatures

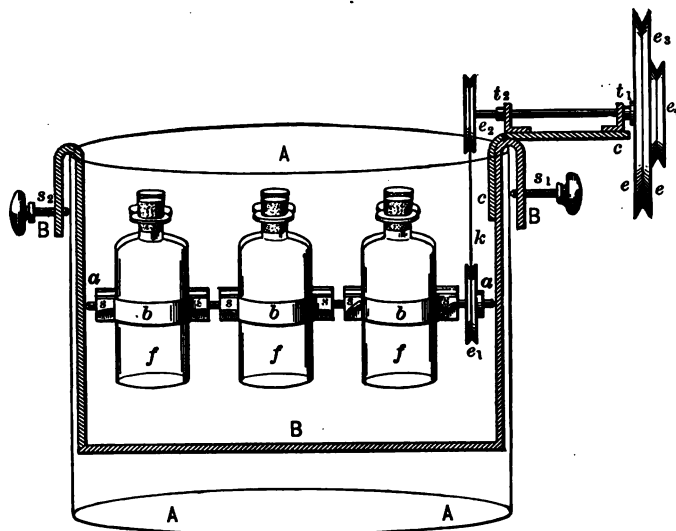


FIG. 13.

for long periods of time. The temperature is observed at which the last trace of the solid goes into solution.

If the first method is employed, the apparatus represented in Figs. 13 and 15 can be used for this purpose.

In Fig. 13 (apparatus of Noyes \*), *BBB* is a copper stirrer that can be fastened into the thermostat (Fig. 1 on p. 11) by means of the screws  $S_1$  and  $S_2$ . The shaft *aa* turns about the points *a* and *a*. This shaft can be made to rotate by connecting the cord pulleys  $e_1$ ,  $e_2$ , and  $e_3$  with a hot-air

\* *Zeitschr. f. physik. Chem.* 9, 603 (1892).

motor. The cone pulley  $e_3e_4$  permits a regulation of the speed of revolution (for example, one revolution per second).

To the axle  $aa$  are soldered six copper rings  $bbb$  into which six flasks  $fff$ , sealed with rubber stoppers, may be fastened by means of screws.

The finely pulverised solid and the liquid are introduced into the flasks, care being taken that a large excess of the former lies at the bottom of the flasks, and is present when saturation has been accomplished. After the bottles are stoppered, the apparatus is set into the thermostat, and the temperature of the same is regulated by using the regulator described upon page 11.

With substances the solubility of which varies greatly with the temperature, great importance is to be attached to the care with which the temperature is kept constant during the experiment.

The shaking is continued from one to three hours. The higher the temperature, the more rapidly will equilibrium (saturation) be established, and the time of the experiment may be proportionately diminished.

In order to be certain that saturation has indeed been reached, two determinations are made,—the first, for example, after two hours, the second after three hours. If both experiments yield the same result, then two hours of shaking suffice in further determinations made at the same temperature. After saturation has been reached, the sediment in the flasks is allowed to settle, the surface of the water in the thermostat is brought just under the necks of the flasks, and, after being carefully dried, the pipette of Landolt (Fig. 14) is dipped into one of the flasks. By means of this pipette, which has been previously dried and

weighed, one can remove, without fear of loss through evaporation, a certain amount of the saturated solution which is to be used for analysis. To do this the ground



FIG. 14.

caps *H* and *A* are removed, and the lower part of the pipette is dipped into the saturated solution. Through suction at *G* the solution enters through *CD* into the expanded part *E* of the pipette. Since the opening of the tube *DC* is very narrow at *B*, solid particles are held back. The glass caps are then replaced and the weight of the filled pipette is determined. After the weight of the saturated solution has been thus determined, it is washed into a flask and analysed.

At low temperatures, where loss through evaporation is less to be feared, instead of the Landolt pipette a  $\frac{1}{2}$ -cm. wide straight glass tube may be used, to which by means of a short rubber tube a smaller glass tube is attached. The latter is about 2 cm. long and drawn out in the middle; a cotton plug serves as a filter.

When through suction the saturated solution has entered the wide tube, the rubber connection is broken and the solution is quickly permitted to flow into a weighing flask which is immediately stoppered and weighed.

If only small amounts of the solid are at our disposal, the apparatus pictured in Fig. 15 (van Deventer-Goldschmidt) for determining solubility offers certain advantages.

*A* is a glass cylinder that can be closed at both ends with the perforated caoutchouc stoppers *S* and *B*.

In this cylinder the solid substance and the liquid are

mixed. The stirring is accomplished by the centrifugal glass stirrer *HAOF* of Witt. This consists of a pear-

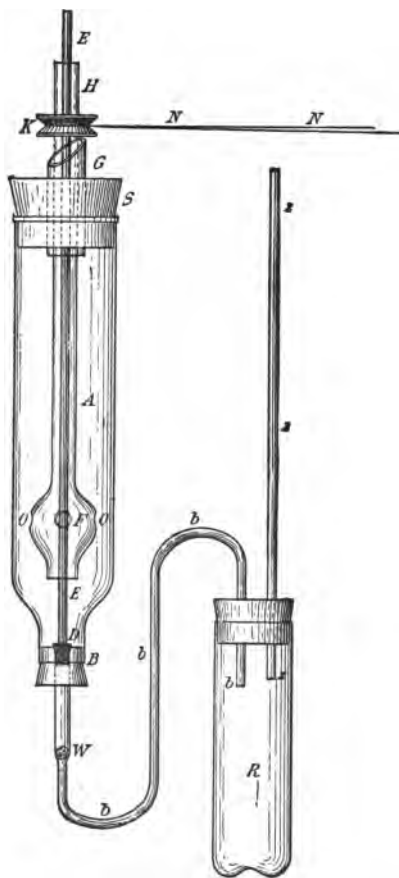


FIG. 15.

shaped glass body *OF* perforated by four openings, each pair of which lie diametrically opposite each other. The

handle *H* of the stirrer passes through the glass tube *G* fastened into the stopper *S*, and is made to rotate rapidly by means of a cord pulley *K*, connected with a hot-air motor. *K* rests upon the obliquely cut tube *G*.

The tube *W* passes through the stopper *B*, and holds at the constriction a cotton plug to serve as a filter. The glass stopper *D*, to which the glass rod *DE* is fused, seals *W* as long as the stirring continues. When saturation is reached *D* is raised by pulling *FD* upwards, and suction is applied at *z*.

The saturated solution, after filtering through *W*, flows into the previously weighed vial *R*; as soon as a sufficient amount has collected therein, the entire apparatus is quickly removed from the thermostat, and *R* is dried and stoppered with a glass stopper. The solution is then weighed and analysed.

At higher temperatures, or in case the liquid employed is volatile, the stirrer is fastened into the cylinder *A* by means of a mercury seal, in such a way that the stirring is not interfered with.

The second of the above-mentioned (see p. 100) methods of determining solubility is used especially when we are dealing with temperatures that lie near or above the boiling-point of the solvent.

Many solubility determinations have been made according to the above-described methods. In Fig. 16 the results with several salts (in water) are represented graphically.

The ordinates give the parts by weight of the salt in 100 parts by weight of water, while the abscissas indicate the temperatures.

Three varieties of solubility can be distinguished in the figure:

1. The solubility increases with an increase in temperature; this is the case most frequently, for example with  $\text{KNO}_3$  and  $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$  (Glauber's salt).

2. The solubility decreases with an increase in temperature; this is the case with anhydrous  $\text{Na}_2\text{SO}_4$  and the

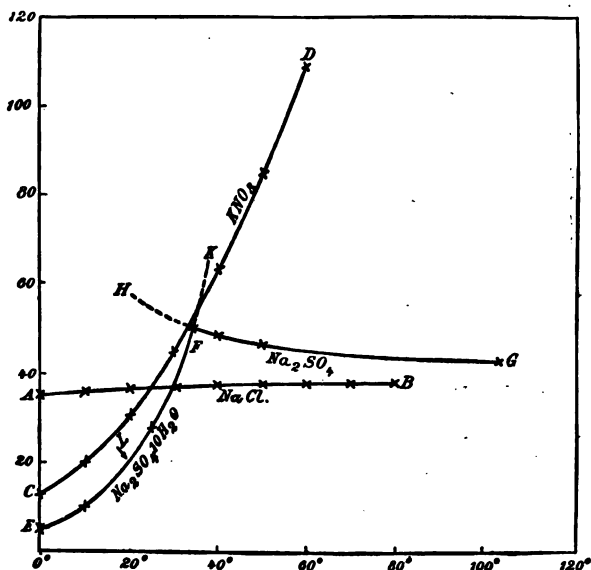


FIG. 16.

calcium salts of many organic acids (calcium succinate, calcium citrate).

3. The solubility does not vary with the temperature; this is approximated by sodium chloride.

We will now consider somewhat more closely the curve that the solubilities of a substance at various temperatures form—the so-called *solubility curve*—remembering that we are dealing with the solubility of a salt in water.



The points  $a$ ,  $b$ , and  $c$  upon the curve in Fig. 17 give the composition of the saturated solution at the temperatures  $t_1$ ,  $t_2$ , and  $t_3$ , that is to say, these points represent the number

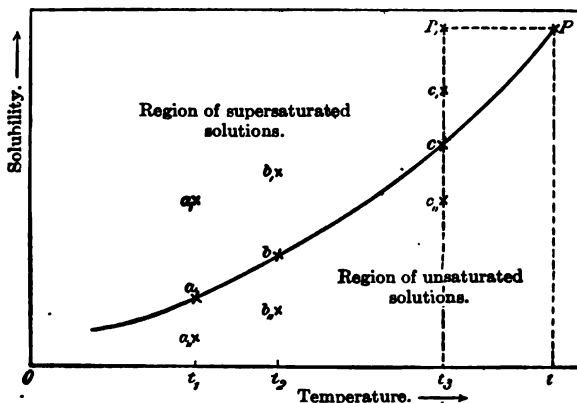


FIG. 17.

of grams of salt that dissolve at these temperatures in 100 g. of water.

The points  $a$ ,  $b$ ,  $c$ , then refer to solutions which at the temperatures  $t_1$ ,  $t_2$ ,  $t_3$  contain a greater amount of the salt per 100 g. of water than they would contain if they had been saturated at the given temperatures. (*Supersaturated solutions*.) The points  $a''$ ,  $b''$ ,  $c''$ , give the constitution of solutions which at the temperatures  $t_1$ ,  $t_2$ ,  $t_3$  contain less salt per 100 g. of water than they would contain if they had been saturated at the given temperatures. (*Unsaturated solutions*.)

The solutions the composition of which is represented by the points on the solubility curve—that is, the saturated solutions—exist at the corresponding temperatures in stable equilibrium. This is not the case with the

supersaturated solutions; these, whenever possible, precipitate their excess of salt and pass into the condition of stable equilibrium. The state of these supersaturated solutions is designated as *metastable*.

How now can we prepare a supersaturated solution, such, for example, as corresponds in composition with the point  $P_1$ ?

If we heat salt and water together up to the temperature  $t$ , at which the last trace of salt just goes into solution, then we say that the solution is just saturated at  $t^\circ$ , and its composition is then represented by the point  $P$ .

If now the solution is carefully cooled until the temperature has fallen to  $t_s$ , care being taken meanwhile that no crystals precipitate out of the solution during the cooling (we are then proceeding along the line  $PP_1$  and not along  $Pc!$ ), then after cooling there is found in the solution at the temperature  $t_s$  as much salt as is represented by the point  $P_1$ , that is, therefore, a larger amount than would be in the solution if it had been saturated at this temperature, for the composition of the solution saturated at  $t_s$  is represented by the point  $C$ .

The solution is therefore now supersaturated at the temperature  $t_s$ .

The same condition of affairs could also have been brought about if, through evaporation, water had been withdrawn from the solution which at the temperature  $t_s$  is saturated, and the composition of which is represented by the point  $C$ . If this is done with care and crystallisation is avoided, the concentration of the solution is increased, and we proceed along the line  $CP_1$  to the point  $P_1$ .

If an extremely small crystal of the dissolved substance or of an *isomorphic* substance (that is a substance which

crystallises in the same crystalline form) is introduced into the supersaturated solution, the metastable condition is broken up through this "germ," and the stable state is established,—enough solid salt crystallises out that the concentration of the solution again corresponds to the point  $c$ ; the solution is again saturated for the temperature  $t_3$ .

If the supersaturated solution is cooled much below its temperature of saturation, the condition of supersaturation can be destroyed even *without* contact with a crystal.

In those cases in which the supersaturation can be broken up by a "germ" of the dissolved substance, the question arises, What amount suffices to call forth the crystallisation? The answer to this question in the case of supersaturated sodium chlorate solutions (a solution of 107 g. of sodium chlorate in 100 g. of water remains supersaturated at room temperature for an indefinite period) was obtained by Ostwald \* in the following way:

Drops of the supersaturated sodium chlorate solution were brought in contact with extremely small amounts of *solid* sodium chlorate, and it was determined what amount of sodium chlorate just sufficed to call forth crystallisation, and what amount was ineffective.

The solid sodium chlorate was diluted by trituration with powdered quartz, the dilutions being prepared in the manner employed by homœopathists.

1 g. of the chlorate was, for example, trituated with 9 g. of powdered quartz; 1 g. of this mixture (containing  $\frac{1}{10}$  g. of the chlorate, therefore) was further trituated with 9 g. of powdered quartz; a mixture then results

\* Zeitschr. f. physik. Chem. 22, 289 (1897).

that contains per gram  $\frac{1}{10} \times \frac{1}{10} = (\frac{1}{10})^2 = \frac{1}{100}$  g. of the chlorate, etc. One gram of the  $n$ th mixture accordingly contains  $(\frac{1}{10})^n$  g. of sodium chlorate.

Drops of the supersaturated sodium chlorate solution were now brought in contact (*inoculated*) with these mixtures. These experiments showed that  $\frac{1}{10}$  milligram of the fifth mixture called forth the crystallisation, while  $\frac{1}{10}$  milligram of the sixth dilution was ineffective. From this it is seen that  $0.0001 \times (\frac{1}{10})^5$  g. =  $\frac{1}{1000000}$  mg. of the solid sodium chlorate suffices for the dissolution of the supersaturation.

We have thus far considered only the case in which we deal with the equilibrium between one solid substance and one liquid. The conditions of equilibrium become somewhat more complicated when we deal with two solids and one liquid, etc. To within fifteen years the explanation of the manifold phenomena in the extensive field of equilibrium was most unsatisfactory, since guiding principles in experimental investigation were absent.

Supported by the so-called *phase rule* \* of Gibbs, Bakhuis Roozeboom, † van't Hoff, ‡ and Bancroft § with their

\* In illustration of the conception "phase" it may be pointed out that when, for example, water and water vapour, or ice and water vapour exist side by side, water and vapour or ice and vapour constitute the phases of the given systems. We therefore deal with three phases in the system, saturated solution and aqueous vapour, namely, solid salt (which lies upon the bottom), solution, and vapour. Each phase constitutes a homogeneous whole, which by mechanical means may be separated from the remaining phases.

† Die Bedeutung der Phasenlehre. Leipzig 1900. Die heterogenen Gleichgewichte vom Standpunkte der Phasenlehre. Braunschweig 1901.

‡ Bildung und Spaltung von Doppelsalzen. Leipzig 1897.

§ The Phase Rule. Ithaca 1897.

pupils have studied the general conditions that determine equilibrium.

#### THE INVERSION TEMPERATURE.

If in the above-described manner we prepare saturated solutions of Glauber's salt ( $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ ) at various temperatures (beginning, for example, with zero degrees), it is found by analysis that between  $0^\circ$  and  $33^\circ$  the solubility of the salt steadily increases with an increase in the temperature. (See curve *EF* in Fig. 16.) If we increase the temperature above  $33^\circ$  and proceed with our solubility determinations, we find that above this temperature the solubility curve *FG* is not continuous with the curve *EF*, but that a break occurs at  $33^\circ$ ,—the change in solubility for each degree suddenly assumes an entirely different value from that which it had before.

Thus the solubility determinations made by Loewel \* furnished the following figures which show how many grams  $\text{Na}_2\text{SO}_4$  per 100 g. of water are present in the saturated solution.

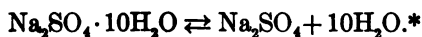
Saturation with $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ .		Saturation with $\text{Na}_2\text{SO}_4$ .	
31.84°	40	32.65°	49.78
32.65	49.78	50	47
Change in solubility per degree.		Change in solubility per degree.	
$\frac{49.78 - 40}{0.81} = 12.1$		$\frac{47 - 49.78}{17.35} = -0.16$	

If now we remove the sediment lying at the bottom of the saturated solution and by analysis determine its composition, we find that we have to deal no longer with  $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$  (Glauber's salt), but with another salt, the anhydrous  $\text{Na}_2\text{SO}_4$ .

\* *Annales de chimie et de physique* (3) 29, 62 (1850); 37, 157 (1853); 49, 32 (1857).

We can therefore say: Above 33° Glauber's salt cannot exist, it is converted into the anhydride. This salt has a solubility of its own (also a corresponding solubility curve *GF*); the break at 33° has its origin, therefore, in the fact that at this temperature a different sediment comes into existence.

If the Glauber's salt has been transformed by heating above 33° into the anhydride (with coincident splitting off of the ten molecules of water of crystallisation) and we cool the newly arisen system to below this temperature, the water of crystallisation will again be taken up by the anhydride, and the hydride, the Glauber's salt, will be re-formed. This reversible process may be expressed by the following equation:



While, therefore, above 33° the Glauber's salt is completely converted into the second system, conversely, below this temperature, Glauber's salt is formed until the second system has entirely disappeared. At 33° both systems can exist side by side. This temperature, above which the Glauber's salt is transformed into the anhydride, is designated the *inversion temperature of the Glauber's salt*.

If the second system is put into a vessel and very slowly cooled to below the inversion temperature, care being taken that "germs" of the first system are entirely excluded, the anhydrous condition can also be maintained below this temperature. The anhydride is then, however,

\* Strictly speaking, the fact should also be brought out in the equation that the anhydride formed forms a saturated solution with the water of crystallisation that is split off. Nevertheless the equation given above represents the general course of the reaction very well.

in the metastable state; an extremely small trace of Glauber's salt suffices to bring about the total inversion into  $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$ . This behaviour brings to mind phenomena with which we became acquainted earlier (see p. 107) in dealing with supersaturated solutions.

We see from Fig. 16 that at the inversion temperature the solubilities of the two systems which can be transformed from one into the other are equal; at this point the solubility curves of the two systems cut each other.

If, for example, we cool a solution saturated with  $\text{Na}_2\text{SO}_4$  at  $35^\circ$  to below the inversion temperature, if germs of  $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$  are excluded, the curve  $GF$  can be followed, that is to say, a saturated solution of  $\text{Na}_2\text{SO}_4$  can be produced below the inversion temperature. The point  $H$ , for example, indicates the constitution of such a solution at  $20^\circ$ . This solution is supersaturated with regard to  $\text{Na}_2\text{SO}_4 \cdot 10\text{H}_2\text{O}$  (for the composition of the saturated solution of Glauber's salt at  $20^\circ$  is indicated by the point  $L$ ); if a crystal of Glauber's salt be introduced into the solution, the sediment will immediately be converted into Glauber's salt, and this salt will crystallise out until the solution contains the amount represented by  $L$ .

The transformations described here for Glauber's salt are found, in general, in other salts holding water of crystallisation. Many another interesting phenomenon connected with the existence of an inversion temperature might be described here, yet we shall rather illustrate by simple examples two of the various methods that can be employed in determining the inversion temperature.\*

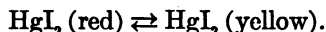
\* See Reicher, *Zeitschr. f. Krystallographie* 8, 593 (1884). E. Cohen, *Zeitschr. f. physik. Chemie* 14, 53 and 535 (1894); 16, 453



Mercuric iodide,  $\text{HgI}_2$ , belongs to the group of *polymorphous (allotropic)* substances, that is substances which can crystallise in various crystalline forms. Two modifications of the mercuric iodide are known—a red which is tetragonal and a yellow which is rhombic.

If the red iodide is heated, it is transformed into the yellow form when the inversion temperature is exceeded. If the yellow form is simply cooled to below the inversion temperature, the red modification is re-formed.

We can represent this process by the equation



Since in this instance the two systems can be clearly distinguished from each other by the differences in their colours, to determine the inversion temperature one need only observe the red iodide in a test-tube while slowly increasing the temperature, and determine at what temperature the change in colour takes place.

The investigations of Rodwell \* and Schwarz † have shown that this takes place at  $126^\circ$ . Above  $126^\circ$  the red iodide is transformed into the yellow, below  $126^\circ$  the yellow is converted into the red.

If, however, the yellow iodide is cooled very carefully to below  $126^\circ$  (with exclusion of crystals of the red form), it continues to exist below this temperature, is then, however, in the metastable condition. The addition of a trace of the

(1895); 25, 300 (1898); 30, 623 (1899); 30, 601 (1899); 31, 164 (1899). van't Hoff, *Bildung und Spaltung von Doppelsalzen*, p. 33.

\* *Philosophical Transactions* 173, 1141 (1882).

† *Preisschrift Göttingen* 1892, p. 15, where references to the literature may also be found.



red iodide calls forth an immediate conversion into the red form. Only at  $126^{\circ}$  can the two forms exist indefinitely side by side,—that is to say, be in equilibrium.

The second method for determining the inversion temperature that is here to be described is the so-called *dilatometrical*. The principle underlying it is that in most inversions the specific volumes (that is, the volume of a gram of the given substance) of the substances present at the beginning and at the end of the inversion are different—that the inversion is accompanied by a change in volume. As an example we will consider more closely the allotropic modifications of tin which have been studied in this direction by Cohen and van Eijk.\*

Casual observation in countries where very low temperatures prevail in winter, as also specially prepared preliminary experiments, had shown that when the universally known white tin is cooled to low temperatures, it is changed into another form having a greyish colour; the latter upon heating can be reconverted into the white form. That the conversion of the white into the grey form is accompanied by considerable expansion is shown by the simple experiment that the white metal becomes covered with innumerable greyish, wartlike swellings (see Fig. 18) when cooled.

The specific volume of the grey tin is therefore greater than that of the white.†

\* Zeitschr. f. physik. Chem. 30, 601 (1899); 33, 57 (1900); 35 588 (1900); 36, 513 (1901), where references to the literature may also be found.

† Since the specific volume is equal to the reciprocal value of the specific gravity, the specific gravity of the grey tin is therefore less than that of the white. In harmony with this, preliminary experiments thus far performed have shown that at  $16^{\circ}$  the specific gravity of the white tin = 7.3, of the grey = 5.8.



Fig. 18.

If, now, we wish to determine the inversion temperature of

grey tin  $\rightleftharpoons$  white tin,

we make use of the *dilatometer* represented in Fig. 19. The inside of the glass tube *A* is filled up with a mixture of grey

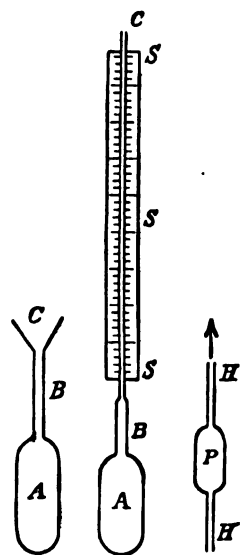


FIG. 19.

and white tin by pouring the mixture through the funnel *C*. The funnel is then cut off at *B* and the small glass capillary *BC* is fused thereto. The vessel *A* and a part of the capillary are now filled with any indifferent fluid (such as oil or petroleum). For this purpose the pipette *HPH*, containing this fluid, is connected with the capillary at *C* by means of a thick-walled rubber tube, and the air is exhausted from *ABCHP* by connecting *H* (where the arrow is shown in the figure) with the hydraulic air-pump. By this means the air-bubbles escape through the liquid into *P*; when the air has been exhausted the connection

with the hydraulic air-pump is broken, and the liquid is permitted to pass into *A* (by holding *HPH* vertical). This procedure is repeated until *AB* is entirely, and the capillary *BC* partially, filled with the liquid. If by accident this stands somewhat too high in the capillary, the excess is removed by introducing (at *C*) a very fine capillary connected with the air-pump.

Behind the capillary *BC* is put a paper (millimetre-paper)

or porcelain millimetre-scale which permits one to read off the height of the liquid in the same.

The dilatometer is now immersed in a thermostat the temperature of which, for example, is  $5^{\circ}$ . After fifteen minutes the apparatus has assumed this temperature. If this lies below the inversion temperature, the meniscus of the liquid will rise in the capillary; for under these conditions grey tin is formed at the expense of the white, and this change necessitates an increase in volume, which must betray itself by a rise of the liquid in the capillary.

If we increase the temperature above the inversion temperature, the grey tin will be converted into the white form, and so bring about a fall of the liquid in the capillary. Through interpolation of the values obtained we can determine the temperature at which the thermostat must be kept in order that the column of liquid in the capillary may show no variations. This temperature is the temperature of inversion, for at this temperature both modifications can exist side by side, without one being converted into the other, that is without the occurrence of a change in volume.

Thus in one experiment the findings were as follows :

Temperature.	Time in Hours.	Rise of the Fluid in the Capillary.	Rise per Hour.
$-5^{\circ}$	25	100	4
0	15	37.5	2.5
5	12	6	0.5
10	17	0.85	0.05
17	15	0.60	0.04
20	24	-0.96	-0.04

While, therefore, at  $17^{\circ}$  the rise per hour amounted to

0.04 mm., at 20° it equalled -0.04 mm. By a simple interpolation we get for the inversion temperature 18.5°

According to this, below 18.5° the grey form of tin is the stable one, while the long-known white form is then metastable. We come, therefore, to the surprising conclusion that all tin objects, such as we are acquainted with in daily life, exist in a state of metastable equilibrium. Only on warm days, when the temperature lies above 18.5°, is their condition a stable one.

Just as we can compel a metastable solution of sodium sulphate, which is supersaturated in respect to Glauber's salt (see *H* in Fig. 16), to assume the condition of stable equilibrium for the given temperature through "inoculation" with a crystal of Glauber's salt, white tin, which below its inversion temperature also exists in metastable equilibrium, can also be made to pass over into the stable grey form, by bringing it in contact (inoculating it) with a crystal of the grey form.\* The nodules upon the tin block pictured in Fig. 18 arose in this manner; if the block is kept at a temperature below 18.5°, they become progressively larger. Since the conversion finally leads to total disintegration of the metal, this phenomenon has received the name of "tin pest."

#### SOLUTIONS OF SOLIDS IN SOLIDS.

The so-called *solid solutions* (van't Hoff †) have up to the present time been studied but slightly. Various substances which have the same crystalline form (*isomorphous substances*) can under various conditions crystallize

\* We cannot here go into greater details; for the references given on p. 113.

† Zeitschr. f. physik. Chem. 5, 322 (1890).

and so form, as *mixed crystals*, a solid solution. In the consideration of the phenomena of diffusion we shall become acquainted with a few other examples of this sort.\*

#### THE INFLUENCE OF TEMPERATURE UPON EQUILIBRIUM.

The general law governing the influence of temperature upon equilibrium was deduced by van't Hoff in 1884 from thermodynamical considerations.† (*The principle of mobile equilibrium.*)

In words this may be stated as follows: Every equilibrium between two different conditions of matter (systems) is, at constant volume, displaced by lowering the temperature towards that system the formation of which evolves heat.

The following statements which may be deduced from the above principle include all possible cases:

1. When the transformation of the first system into the second takes place with the production of heat,‡ an increase in temperature will be followed by a displacement of the equilibrium towards the side of the first system.
2. When the transformation of the first system into the second takes place with an absorption of heat, an in-

\* References to the literature may be found in Bodländer, *Neues Jahrbuch für Mineralogie, Geologie und Paläontologie, Beilage 12, 52* (1898).

† *Etudes de Dynamique chimique*, Amsterdam 1884. See van't Hoff-Cohen, *Studies in Chemical Dynamics*, Leipzig and London 1896, translated by Dr. Thos. Ewan.

‡ Chemical actions that take place with heat production, those, therefore, in which heat is set free, are termed *exothermic*; those which occur with heat absorption, in which, therefore, heat is absorbed, are termed *endothermic*.

crease in temperature will be followed by a displacement of the equilibrium towards the side of the second system.

3. When the transformation of the first system into the second occurs without caloric effect, then an increase in temperature will be followed by no displacement of the equilibrium.

To illustrate the use of these statements we shall apply them to a few of the subjects before discussed.

If we consider the decomposition



and ask toward which side the equilibrium will be displaced if the temperature is increased, we must first answer the question, Does the transformation of the first system ( $\text{CaCO}_3$ ) into the second ( $\text{CaO} + \text{CO}_2$ ) occur with heat production or heat absorption? Now calorimetrical measurements have shown that the dissociation of calcium carbonate into calcium oxide and carbon dioxide is an endothermical process. We can therefore, by making use of the law of mobile equilibrium, at once say that through an increase of temperature the equilibrium between  $\text{CaCO}_3$ ,  $\text{CaO}$ , and  $\text{CO}_2$  will be displaced towards the side of the second system, which is to say, therefore, that through an increase in temperature more calcium oxide and carbon dioxide will be formed.

An interesting example of the application of the above propositions is furnished by the equilibrium between solids and liquids,—for example, by the solution equilibrium between a salt and water. We have seen that the solubility of salts can increase, decrease, or remain constant with an increase in temperature.

We deal here with an equilibrium that can be represented by the equation



If we wish to know how the solubility of a given salt varies with the temperature, that is to say, whether the same increases, decreases, or remains constant with an increase in temperature, we have to ask: Does heat production accompany the transition of the first system (salt+water) into the second (saturated solution), or does the change take place with heat absorption, or is no caloric effect demonstrable?

If heat is produced, that is to say, if the heat of solution\* of the salt has a positive value, then with an increase in the temperature the equilibrium will be displaced towards the side of the first system (salt+water), and salt will be precipitated from the solution: the solubility decreases with an increase in temperature.

This happens, for example, in the case of  $\text{Na}_2\text{SO}_4$  (anhydrous) and the calcium salts of many organic acids (see p. 105).

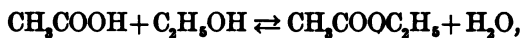
If the transition of the first system (salt+water) into the second (saturated solution) is accompanied by an absorption of heat, then the solubility of the given salt will increase with an increase in temperature, as is the case with

\* We deal here with the heat of solution produced when a mol of salt dissolves in a solution which at the temperature of the experiment is almost saturated, that is to say, with the heat production, which is designated the *theoretical heat of solution* to distinguish it from that which is produced when a mol of salt is dissolved in pure water. The latter is called the *heat of solution* of the salt.



the largest number of salts, for example Glauber's salt, potassium nitrate, etc. The solubility undergoes no change with an increase in temperature when the production of heat in the transition equals zero. The latter is approximated in the case of sodium chloride.

That the equilibrium



as was said before (see p. 74), undergoes no change when the temperature is increased, is explained by the fact that the production of heat in this transformation equals zero.

## EIGHTH LECTURE.

### The Friction of Liquids.

SINCE this property of liquids is of importance to the physiologist also, as recent investigations have demonstrated anew, I wish to deal for a moment with the phenomena that come under this heading.

If the form of a liquid is altered, or the liquid particles change their relative positions, energy is required, since the particles of a liquid stick to each other in a peculiar way, and this force (internal friction, viscosity, tenacity, transpiration) has to be overcome in order that the change in form, or the movement, may occur.

The laws that govern the movement of liquids in tubes were first exhaustively studied for practical purposes by the engineer Hagen\* (1839) and the physician Poiseuille.† The latter sought to become more closely acquainted with the flow of blood in the animal body (hæmodynamics). Just as in the days of iatrochemistry, when physico-chemical investigations were made almost entirely in conjunction with medicine, we see here another illustration of the reciprocity that exists between the practical things of life and science.

The empirically established laws of Hagen and Poi-

\* Poggendorffs Annalen 46, 437 (1839).

† Annales de Chimie et de Physique (3) 7, 50 (1843); (3) 21, 76 (1847).

seuille were later deduced from theoretical considerations and confirmed by Stokes.\*

It was found that when a liquid flows through a long, small-calibred cylindrical tube, the wall of which it wets, the volume ( $V$ ) of the liquid that escapes in the unit of time may be expressed by the following:

$$V = \frac{\pi D r^4}{8 l \eta}.$$

Herein  $\pi = 3.1415 \dots$ ,  $D$  is the pressure under which the liquid escapes,  $r$  the radius of the tube,  $l$  the length of the same, and  $\eta$  a constant for the given liquid dependent upon the temperature and designated the coefficient of internal friction (viscosity coefficient).

This coefficient is equal to the work required to move in one second two liquid surfaces of 1 sq. cm. surface parallelly over each other, the same distance as the distance between the two surfaces.

If we determine the value of  $\eta$  in (1), we find

$$\eta = \frac{\pi D r^4}{8 l V}. \quad (2)$$

The greater the value of  $\eta$ , the more viscid we say is the given liquid,—the greater is its tenacity. If we wish to determine  $\eta$  by the above equation, the liquid is permitted to flow, under a definite pressure ( $D$ ), through a tube the radius ( $r$ ) and the length ( $l$ ) of which have been very accurately determined, and the amount of liquid ( $V$ ) escaping per second is measured.

Such determinations have actually been made. Since

\* Cambridge Philosophical Transactions (3) 8, 304 (1847)

the exact determination of the radius of the tube is by no means an easy task, and since the friction coefficient is proportional to the fourth power of the radius of the tube, a slight error in the determination of  $r$  will effect a considerable error in the value of  $\eta$ .

In many cases, therefore, we are content to determine only the so-called *relative viscosity*, that is to say, the relation between the friction coefficient of the given liquid and that of water at the same temperature.

The use of the simple viscosimeter of Ostwald (Fig. 20) furnishes a convenient means of attaining this end. The capillary  $db$  through which the liquid flows is connected with the bulbs  $k$  and  $e$ . A definite volume of water (2 to 3 c.c.), measured by means of a small pipette, is introduced into the bulb  $e$  and suction is applied at  $a$ , so that  $k$  is filled and the water rises to above the line  $c$  marked on the glass. The liquid is then permitted to flow out through  $db$ ; by means of a stop-watch (divided into  $\frac{1}{4}$  seconds) the times are noted at which the surface of the water passes the marks  $c$  and  $d$ . During the experiment the entire apparatus is immersed in a thermostat, since the viscosity varies with the

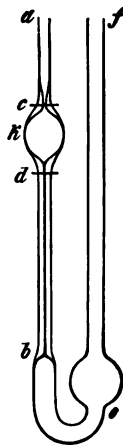


FIG. 20.

temperature, decreasing about 2 per cent with each degree of temperature increase. The experiment is then repeated with the liquid the viscosity of which is to be determined.

It is to be noted that the water (or the liquid) does not flow out under constant pressure; the pressure progressively diminishes during the outflow, yet this can be taken into account in the calculation.

The calculation, into which we cannot enter more closely here, yields the following.

If we represent the time occupied by the water in falling from  $c$  to  $d$  by  $t_0$ , and if  $s_0$  is the specific gravity of the water at the temperature of the experiment,  $\eta_0$  the friction coefficient of the water at this temperature, and the corresponding values of the liquid the viscosity of which we wish to determine are equal to  $t$ ,  $s$ , and  $\eta$ , then

$$\eta : \eta_0 = st : s_0 t_0,$$

or

$$\eta = \eta_0 \frac{st}{s_0 t_0}.$$

If we take the friction coefficient of the water at the temperature of the experiment as equal to unity (we can do this since we only wish to determine how many times the viscosity of the liquid is greater than that of water at the same temperature), then

$$\eta = \frac{st}{s_0 t_0}.$$

In the calculation of  $\eta$  we have to determine, besides the times required for the outflow of the liquids, the specific gravity of the water and that of the liquid under investigation at the temperature of the experiment.

The apparatus illustrated herewith (Fig. 21), a somewhat modified pyknometer of Sprengel-Ostwald,\* can be used for this purpose.

The part  $b$  holds 5–20 c.c. The capillary tubes  $a$  and  $e$  have everywhere the same diameter.  $a$  is dipped into the liquid the specific gravity of which is to be determined, and suction is applied at  $e$ . When the apparatus has been filled, it is hung into a thermostat, and after the temperature has become uniform the position of the liquid in  $a$  and

\* I am indebted to my colleague, Prof. Holleman of Groningen, for calling my attention to this modification which originated with J. F. Eijkman (Recueil des Travaux chimiques des Pays-Bas 13, 24 (1894)). See also Holleman, Recueil 19, 85 (1900).

*e* is read off upon the scale, which is graduated into half-millimetres. If now the volume of one centimetre of the divisions has been determined once and for all by weighing with water, then the volume of any liquid in the pyknometer is known; \* when further, through weighing, the weight of the same has been determined, the specific gravity can be calculated in the customary way.

The following table gives an idea of the viscosity of several pure substances. If we consider the viscosity of water as equal to one, then at the same temperature that of

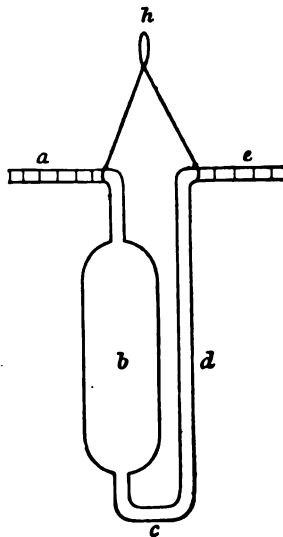


FIG. 21.

Methyl alcohol	=0.63
Ethyl alcohol	=1.19
Ethyl acetate	=0.55
Acetic acid	=1.28

Even though the extensive investigations that have been made in this direction since the work of Hagen and Poiseuille have led to only a few generalisations, yet several simple relations between the amount of indifferent substances contained in dilute solutions and the relative

\* With volatile substances this contrivance possesses the great advantage that the vaporisation occurs slowly, if care is taken that the liquid does not come too closely to the ends of the capillaries.

friction coefficients of the same have been found by Arrhenius.\*

Thereby the strange fact has come to light that nearly all aqueous solutions of the substances examined have a higher friction coefficient than the water itself, while many of the dissolved substances in the pure state have a lower friction coefficient than water. So, for example, an aqueous solution of the mobile sulphuric ether has a greater viscosity than the much less mobile water.

Even though the studies of Poiseuille, as has already been said, were intended originally for the solution of physiological problems, investigations upon the internal friction of animal fluids were resumed only much later by Haro,† Ewald,‡ and Lewy.§ These measurements were, however, all made upon defibrinated blood and so do not justify a conclusion regarding the viscosity of unaltered living blood.

Hürthle and Opitz || have recently conducted very careful experiments upon the viscosity of the blood of various animals. The determinations were made at 37°. The authors believed that the ordinary methods could not be employed, since blood, very soon (several minutes) after being shed, suffers certain changes that exert an important influence upon its viscosity.

To overcome the difficulties hence arising, they

\* *Zeitschr. f. physik. Chem.* 1, 285 (1887); Reyher, *ibid.* 2, 744 (1888); Wagner, *ibid.* 5, 31 (1890); Kanitz, *ibid.* 22, 336 (1897); Euler, *ibid.* 25, 536 (1898).

† *Compt. rend.* 83, 696 (1876).

‡ *Dubois-Reymonds Archiv, Physiol. Abt.* 1877, 208 and 1878, 536.

§ *Pflügers Archiv* 65, 447 (1896).

|| *Ibid.* 82, 415 (1900).

brought the outflow capillary in direct connection with the carotid of the animal experimented upon, and used the pulsating blood pressure as the pressure under which the outflow took place. Preliminary experiments had shown that the formula of Poiseuille holds also under these conditions. The very complicated apparatus constructed by them for this purpose we shall not describe more closely at this point. A few months ago Hirsch and Beck \* succeeded in handling the same problem experimentally by using a somewhat modified form of the Ostwald viscosimeter. By this the entire operation has been greatly simplified, and the universal employment of this viscosimeter as a clinical instrument does not seem impossible, once the relations between the viscosity of the blood (or other animal fluids) and other properties of the same have been studied more closely.

Hirsch and Beck experimented with living human blood at 38°,—that is, therefore, in the proximity of the normal body temperature. The apparatus (Fig. 22) consists of the hand-bellows *A*, the calcium chloride tube *B*, the pressure-bottle *C*, the open manometer *D*, the thermostat *E*, and the viscosimeter *F*. The pressure-bottle is covered with felt to guard against heat radiation, and the manometer, in order to render it more delicate, is filled with benzol distinctly coloured with some organic dye. As a thermostat the apparatus illustrated in Fig. 1 (p. 11) may be used. The somewhat modified Ostwald viscosimeter is illustrated in Fig. 23. Since blood coagulates very rapidly, the viscosimeter must be filled quickly. For this reason the

\* Deutsches Archiv für klin. Medizin 69, 503 (1901), where references to the older literature upon hæmodynamics may be found.



occlusion-tube *V* is ground into *S*. The capacity of the U-shaped part as compared with that of the upper expanded part *G* is such that a sufficient amount of blood for the experiment is present when its surface is on a line with the

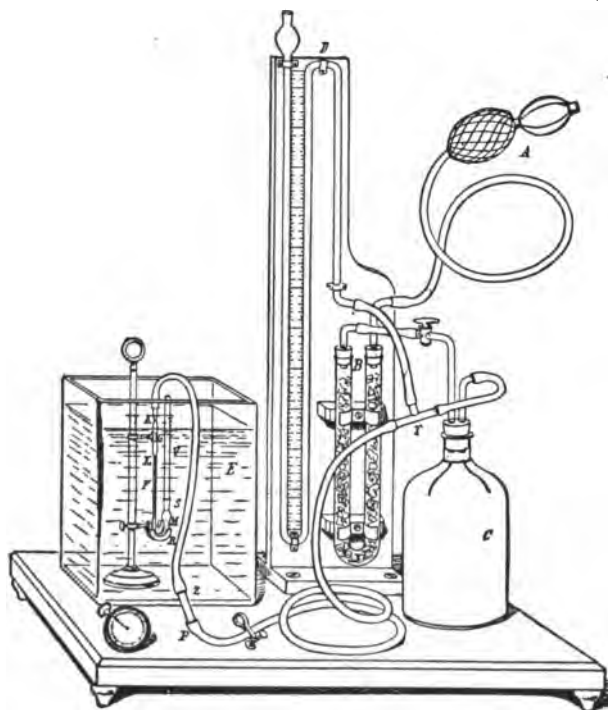


FIG. 22.

beginning of the bulb-shaped expansion at *M*. The capacity of the tube *G* is about  $\frac{1}{2}$  c.c.; the diameter of various capillaries ranges between 0.25 and 0.35 mm. Care should be taken that the apparatus is set up perpendicularly.

The experiment is made in the following way: After the

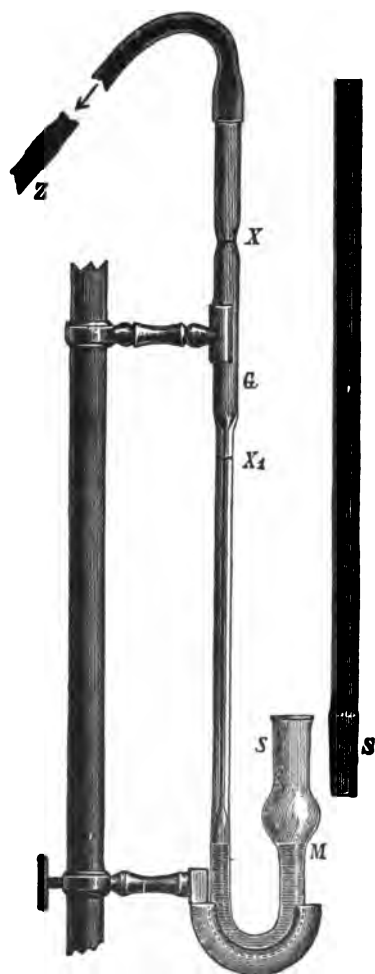


FIG. 23.

rubber tube connection has been broken at *P* and the arm leading to the T tube has been closed with a pinch-cock, any desired pressure, such as about 400 mm. of water = 452 mm. of benzol (specific gravity 0.88) is established. The thermostat is then set at the temperature of 38°.

The viscosimeter connected with the stand and the suction-tube *Z* is kept in an air-bath of the same temperature. The occlusion-tube is removed, its ground end lightly vaselined, and laid aside ready for use.

Through a small cut in the skin a vein is laid bare in the forearm, and a glass capillary of the form shown on p. 133 (Fig. 24) is introduced into the vein for the removal of blood. After the first few drops have been thrown aside, the blood is permitted to flow into the U-shaped part of the apparatus to the point indicated above, the occlusion-tube is put into place, and the apparatus is set into the thermostat. The blood is now sucked to a point above the mark *X*, the suction-tube is connected with the tube leading to the pressure-bottle, and the pinch-cock is opened with one hand, while with the other the stem of a  $\frac{1}{4}$ -second stop-watch is pressed as soon as the surface of the blood passes the mark *X*. When the lower mark *X*<sub>1</sub> is passed, the stem of the watch is again pressed, while the pinch-cock is at the same time allowed to close; the time is noted, it is quickly determined whether the pressure has remained constant, and suction is again made for another measurement. With the same specimen of blood two to six determinations may be made in this way. The apparatus is cleaned by rinsing with dilute caustic soda or sodium carbonate followed by distilled water, and dried in a drying-oven.

In order to calculate the relative viscosity of the blood

( $\eta$ ) compared with that of water at 38°, the specific gravity of the blood ( $s$ ), as also that of water at 38°, and the time of outflow of the latter at this temperature, would have to be determined (see p. 126).

To overcome the difficulties that would accompany the determination of the specific gravity of the blood used in each experiment Hirsch and Beck, when very great accuracy is not required, determine once and for all the time of outflow ( $t_0$ ) at 38° of a liquid the specific gravity ( $s_0$ ) of which is about equal to that of the blood. They use anilin. If the relative viscosity of the anilin at this temperature compared with water at 38° has been determined in the Ostwald viscosimeter and has been found to equal  $\eta_0$ , then (since  $s = s_0$ )

$$\eta = \eta_0 \frac{t}{t_0},$$

where  $t$  is the time of outflow of the blood in their apparatus. From this  $\eta$  can at once be calculated.

As an average value for human blood (specific gravity 1.045 to 1.055) it was found that  $\eta = 5.1$  at 38°, when the viscosity of water at this temperature is taken as unity. For dog blood was found, at the same temperature, 4.7, for cat blood 4.2 (Hürthle and Opitz). Too great value is, however, not to be attached to these figures, since it was found that not only individual differences exist, but that the nature of the food also has a distinct effect in animals.

Haro and Ewald found that the viscosity of the (defibrinated) blood decreases with an increase in temperature, while Lewy states that it remains almost constant from 27–45° and then rapidly diminishes.

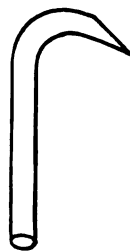


FIG. 24.

The investigations of Opitz showed that between 15° and 40° the viscosity decreases with an increase in temperature (as is also the case with simple liquids), but that the decrease per degree of difference in temperature is almost constant.

Now such a regular increase is not found in the case of water or aqueous salt solutions; with these the viscosity diminishes more rapidly at higher temperatures than at lower. Since serum in this respect behaves like water, the regular decrease in the viscosity of the blood must be attributed to the presence in the blood of the solid substances, which with an increase in temperature suffer certain (as yet unknown) changes that compensate in part for the rapid decrease in the viscosity of the serum.

The procedure described above makes the solution of many an important problem, such as the determination of the relationship existing between the viscosity of the blood and the secretion from the kidneys, accessible to experiment.\*

\* Jacoby, Lecture to the Mediz. Gesellsch. zu Göttingen, Jan. 10, 1901. Abstract in *Deutsche med. Wochenschr.* 27 (1901), *Ver- einsbeilage*, p. 63.

## NINTH LECTURE.

### Osmotic Pressure.

If a salt solution \* is put into a vessel and pure water is carefully poured upon it, after the whole has been left entirely undisturbed for some time it is found that the salt has distributed itself through the entire solution; the movement of the dissolved substance (here the salt) does not cease until it has distributed itself uniformly throughout the solution.

The phenomenon described here, the movement of the particles of dissolved substance from places of higher concentration in the liquid to places of lower concentration, is called the *diffusion* of the substance. We shall later discuss this phenomenon more fully. Here we ask first of all, What is the cause of the diffusion; how is it brought about?

If we wish to render apparent the movement of the dissolved substance in the liquid, we can accomplish this by separating the place of higher concentration from that of lower concentration by a wall which will give passage to the liquid but not to the dissolved substance. Such a wall is termed *semi-permeable*.

The dissolved substance in its movement through the liquid will now be stopped by this wall, and in consequence

\* When we here and in what is to follow, for the sake of brevity, speak of *salt* and *water* (salt solution), we generally mean thereby any substance that is dissolved in the given liquid.

will exert a pressure upon it. This pressure we term the *osmotic* (from ὠθηέω = to drive through) pressure of the solution.

The first observations upon this subject date from Nollet\* (1754), who used a bladder as a semi-permeable wall. Nollet filled a glass, the bottom of which was made of a bladder, with spirits of wine, and found that water passed through the bladder into the alcohol as soon as he dipped the glass into pure water. If the glass was closed above, the bladder burst after some time because of the pressure produced within the glass.

The significance of this diffusion in the animal organism was also recognised by Nollet, yet his experiments, as also those of the physiologists who studied this phenomenon up to the middle of the nineteenth century, led to no general conclusions.†

Practical methods of producing semi-permeable walls were brought forward by the celebrated wine merchant and chemist, Moritz Traube, in his "Experimente zur Theorie der Zellenbildung und Endosmose" ‡ (1867), yet the first quantitative osmotic measurements were described by Pfeffer in his "Osmotische Untersuchungen" § (1877). Pfeffer succeeded in firmly supporting the readily broken semi-permeable walls of Traube, the so-

\* Leçons de physique expérimentale, Amsterdam 1754.

† For the old literature concerning this subject see Vierordt, Archiv für physiologische Heilkunde von Roser und Wunderlich 5, 479 (1846). Also Jagielsky, Programm des Gymnasiums Trzemeszno, 1859.

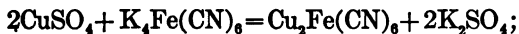
‡ Archiv f. Anatomie und Physiologie 87, 1867. See also: Gesammelte Abhandlungen von Moritz Traube, Berlin 1899. 200-206; 213-217.

§ Leipzig 1877.

called *precipitation membranes*, in the pores of unglazed vessels of earthenware.

Such a membrane may be made in the following way: A Pasteur-Chamberland filter is sawed in half with a scroll-saw. The resulting small clay cylinder is closed with a perforated rubber stopper through which is passed a glass tube. The cylinder is dipped into dilute hydrochloric acid, which is sucked through the wall of the cylinder by a hydraulic air-pump, in order to remove any caolin dust that might choke up its pores. In a similar way the cylinder is then rinsed with water. A beaker is now filled with a solution of potassium ferrocyanide (139 g. per litre), the cylinder is dipped into it, and the solution is sucked through its wall. After the cylinder has been again rinsed in water it is dipped into a second beaker containing a copper sulphate solution (249 g. of the salt per litre), the inside of the cylinder being also filled with the solution.

A layer of copper ferrocyanide is now deposited within the wall of the cylinder



this precipitate of copper ferrocyanide constitutes the semi-permeable precipitation membrane which is permeable for water but impermeable for salts.—Yet we must at once point out the fact that the latter statement is not strictly true. A certain amount of most substances always migrates through this wall,\* and only for the “membranogenous”

\* See Walden, *Zeitschr. f. physik. Chem.* 10, 699 (1892), where references to the literature may be found. See also Naccari, *Rendiconti della Accademia dei Lincei* 6, 25 (1897). Ponsot, *Bulletin de la Société chimique de Paris* (3) 69, 9 (1895). Flusin, *Compt. rend.* 131, 1308 (1900); 132, 1110 (1901). Morse and Horn, *Journal Amer. Chem. Society* 26, 80 (1901).



salts, in this instance, therefore, the potassium ferrocyanide and the copper sulphate, is the membrane truly impermeable.

Other solutions can be used in making such membranes, such as potassium ferrocyanide, with a zinc salt. The semi-permeable wall then consists of zinc ferrocyanide.

Membranes of Prussian blue or calcium phosphate have also been used by Pfeffer; yet the best results are obtained with copper ferrocyanide.

If we introduce a sugar solution into a cell *C* (Fig. 25) prepared in this manner, and close it with the stopper *S*

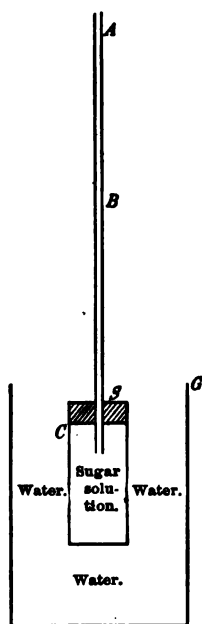


FIG. 25.

which is perforated by the tube *AB*, then, when *C* is dipped into pure water, the sugar endeavours to pass from the place of higher concentration (the solution) to that of lower concentration (the water without the cell).

But this movement is opposed by the semi-permeable membrane, and in consequence the sugar exerts a pressure upon the membrane. Since this wall, however, is unyielding, and so resists the pressure, a pull is exerted upon the water by the solution, which tends to dilute the latter. This comes to pass if the solution enters the tube, and the water from *G* streams through the membrane into the cell and dilutes the solution. This process goes on until the hydrostatic pressure resulting

in *AB* prevents the further entrance of water. When

equilibrium has been established, this hydrostatic pressure is equal to the osmotic pressure of the solution.

Conversely, however, the latter may be measured by ascertaining the hydrostatic pressure which exists when equilibrium is established.

Pfeffer measured the osmotic pressure of sugar solutions of various concentrations with a mercury manometer, and obtained with such an *osmometer* the following results:

## TEMPERATURE ABOUT 14°.

Grams sugar per 100 g. water.	Osmotic pressure in mm. of mercury.
1.0 .....	535
2.0 .....	1016
2.74.....	1518
4.0 .....	2082
6.0 .....	3075

Pfeffer studied the influence of temperature upon the osmotic pressure of a one per cent sugar solution.

Temperature.	Osmotic pressure in mm. of mercury.
{ 14.2.....	510
{ 32.0.....	544
{ 6.8.....	505
{ 13.7.....	525
{ 22.0.....	548
{ 15.5.....	520
{ 36.0.....	567

The values contained in brackets were always obtained with the same osmometer.

We therefore deal here with very considerable pressures.\*

The data collected by Pfeffer solely for the purposes of plant physiology lay unused for about eight years, when

\* See Errera, Sur la Myriotonie, Bulletins de l'Académie Royale de Belgique No. 3, 1901. Cited from reprint.

they were brought to light again by van't Hoff in the presentation of his theory of osmotic pressure. This was communicated to the Swedish Academy of Sciences in Stockholm\* in an essay entitled "Lois de l'Équilibre chimique dans l'État dilué, gazeux ou dissous," later published in a somewhat different form under the title "Die Rolle des osmotischen Druckes in der Analogie zwischen Lösungen und Gasen," in the *Zeitschrift für physikalische Chemie*.†

In these essays van't Hoff deduces from thermodynamical considerations the following law:

At constant temperature the osmotic pressure of dilute solutions is proportional to the concentration of the dissolved substance. (Law of Boyle-van't Hoff.) This law is the analogue of Boyle's law for dilute gases, which states that at constant temperature the (gas) pressure of a gas is proportional to its concentration.‡

In order to test the correctness of this law van't Hoff used the measurements of Pfeffer. It must be remembered, however, that the temperatures at which Pfeffer made his observations were not kept absolutely constant, but varied between 13.2 and 16.1.

The following table shows in how far the measurements coincide with the law stated above:

\* Kongl. Svensk. Vetenskaps-Akademiens Handlingar 21, 17 (1886). In the German by G. Bredig. Ostwalds Klassiker d. exakten Wissenschaften No. 110, Leipzig 1900.

† *Zeitschr. f. physik. Chem.* 1, 481 (1887). Studies in Chemical Dynamics. Revised and enlarged by Ernst Cohen. Trans. by Thomas Ewan Easton. Amsterdam and London 1896.

‡ It will be noted that the concentration is inversely proportional to the volume.

<i>C</i> Concentration of the solution.	<i>P</i> Osmotic pressure in mm. of mercury.	$\frac{P}{C} = \text{constant.}$
1.0%.....	535	535
2.0.....	1016	508
2.74.....	1518	554
4.0.....	2082	521
6.0.....	3075	513

The relation  $\frac{P}{C}$ , which according to theory should have a constant value, does indeed approach the same. This means, for example, that doubling the concentration doubles the osmotic pressure.

Such a distinct analogy between the osmotic pressure of a dilute solution and the gas pressure of dilute gases having here been found, it lay at hand to ask whether an analogue of the law of Gay-Lussac also existed.

For dilute gases this law may be stated as follows: At constant volume the pressure of a given weight of gas increases as the absolute temperature.

If we make the expansion coefficient of gases  $\left(\frac{1}{273}\right)$  equal to  $\alpha$ , then at  $t^\circ$ , according to Gay-Lussac,

$$P_t = P_0(1 + \alpha t), \quad (1)$$

wherein  $P_t$  and  $P_0$  represent the pressures of the gas at the temperatures  $t^\circ$  and  $0^\circ$ .

If we calculate the temperatures according to the absolute temperature scale—consequently from  $-273^\circ$  as zero—then the absolute temperature  $T$  which corresponds with  $t^\circ$  is

$$\begin{aligned} T &= t + 273, \\ t &= T - 273, \\ 1 + \alpha t &= 1 + \frac{1}{273}(T - 273), \\ 1 + \alpha t &= \frac{T}{273}. \end{aligned}$$

Equation (1) then assumes the following form:

$$P_t = P_0 \frac{T}{273}$$

The law of Gay-Lussac may consequently also be thus expressed: At constant volume the pressure of a gas is proportional to the absolute temperature. This form of the law is also often used.

Van't Hoff indeed found that such an analogous law could be deduced for dilute solutions, and found it supported, as we shall see, by Pfeffer's measurements. The law for dilute solutions is as follows: At constant volume the osmotic pressure of dilute solutions increases as the temperature, or also: The osmotic pressure of dilute solutions is proportional to the absolute temperature. (Law of Gay-Lussac-van't Hoff.)

If now the osmotic pressure  $P_0$  has been determined at  $0^\circ$ , then it can be calculated for  $t^\circ$  by the equation

$$P_t = P_0 \left(1 + \frac{1}{273} t\right).$$

The following table contains a few of Pfeffer's measurements and the calculations of van't Hoff corresponding thereto:

	Pressure in mm. of mercury.	Tempera- ture.	Tempera- ture.	Pressure.	
				Ob- served.	Calcu- lated.
Sodium tartrate.....	1564	36.6°	13.3°	1432	1443
	983	37.3	13.3	908	907
Cane-sugar.....	544	32.0	14.15	510	512
	567	36.0	15.5	521	529

The law of Avogadro for dilute gases is: Under equal pressure and at the same temperature equal volumes of all gases contain the same number of molecules. This may also be applied to dilute solutions, when it assumes the following form:

At the same osmotic pressure and the same temperature equal volumes of all dilute solutions contain the same number of molecules. (Law of Avogadro-van't Hoff.)

But besides this it can be proved that this number of molecules is equal to that contained in the same volume of a gas under the same pressure and at the same temperature.

The law thus expanded may now be stated in the following form: The osmotic pressure of a given weight of dissolved substance is equal to the gas pressure that the substance would exert were it in the gaseous state, and contained in the same volume as that occupied by its solution.

Van't Hoff tested this law also by Pfeffer's measurements. The following table contains the data bearing upon this question.

Under  $P_0$  are given the osmotic pressure (in atmospheres) observed in a one per cent sugar solution, under  $P_g$  the gaseous pressures which the same amount of sugar (1 g.) would exert at the corresponding temperature if it were contained in a volume equal to that of the solution. It must be remembered that 1 g. of sugar + 100 g. of water forms a solution which at  $0^\circ$  has a volume of 100.6 c.c.

Temperature.	$P_0$ .	$P_g$ .
6.8°.....	0.664	0.667
13.7.....	691	683
14.2.....	671	685
15.5.....	684	688
22.0.....	721	703
32.0.....	716	727
36.0.....	746	736

While, therefore, at  $6.8^\circ$ , for example, the osmotic pressure of a one per cent sugar solution amounts to 0.664 atmosphere in the Pfeffer osmometer, calculation yields the

result that the same amount of sugar (1 g.) in the volume in which it is contained in the solution (100.6 c.c.) would theoretically exert in the gaseous state a pressure of 0.667 atmosphere. The agreement is a very satisfactory one when it is remembered how difficult it is to produce absolutely semi-permeable membranes (see p. 137).

How now was the pressure, 0.667 atmosphere, given above, calculated? We deal here with the answer to the question, What pressure would 1 g. of sugar exert in the gaseous state if it could be vapourised at 6.8°, and if the volume of the resulting gas amounts to 100.6 c.c.?

It must be pointed out, first of all, that a mol of any gas at 0° and 760 mm. pressure occupies a volume of 22.4 litres; this value is obtained by remembering that 1 litre of hydrogen at 0° and 760 mm. pressure weighs 0.09 g., and that a mol of this gas (= 2.016 g.) under the same conditions consequently occupies a volume of  $\frac{2.016}{0.09} = 22.4$  litres. Since, according to Avogadro, at the same temperature and at the same pressure the same number of molecules are found in the same volume, a mol of any gas (at 0° and 760 mm.) will occupy this volume.

Consequently 342 g. of sugar (the molecular weight of sugar  $C_{12}H_{22}O_{11} = 342$ ) in the gaseous state at 0° and 760 mm. pressure would also occupy a volume of 22.4 litres. 1 g. of sugar at 0° and 760 mm. would consequently fill a space of

$$\frac{22.4}{342} \text{ litres} = \frac{22400}{342} \text{ c.c.} = 65.5 \text{ c.c.}$$

If we calculate this volume upon the basis of 100.6 c.c., then the corresponding pressure ( $X$ ) at 0°, according to the law of Boyle, may be calculated from the following proportion:

$$100.6 : 65.5 = 1 : X.$$

$$X = \frac{65.5}{100.6} = 0.651 \text{ atm.}$$

The gaseous pressure of the sugar, if it existed as a gas at  $t^\circ$ , would consequently be

$$0.651(1 + \alpha t) \text{ atm.,}$$

where  $\alpha$  is the expansion coefficient of gases, =  $\frac{1}{273}$ .

If now we put  $t = 6.8$ , this pressure is found to rise to 0.667 atm., the value given in the table.

We have already pointed out the fact that the membranes of the Pfeffer osmometers are always more or less permeable for the dissolved substance; for accurate measurements of osmotic pressure these can therefore not be employed; to this is to be added that precipitation membranes cannot bear high pressures, but are ruptured relatively easily.

The methods employed for exact measurements are for these reasons all indirect ones.

First of all we shall consider a few physiological methods of (indirectly) measuring osmotic pressures.

*a. The Determination of Osmotic Pressure by Plasmolysis.\**

Solutions which at the same temperature have the same osmotic pressure are termed *isosmotic* or *isotonic* solutions.

In the method of *plasmolysis* described by Hugo de Vries,† the endeavour is made to find a solution having a concentration which has the same osmotic pressure as the cell-sap of certain plant-cells,—in other words one that is isotonic with this cell-sap.

If now, while using the same plant-tissues, this concentration is determined for solutions of various substances, we know that the concentrations found are also isotonic when compared with each other, and the results will be

\* See Fr. von Rysselberghe: Réaction osmotique des cellules végétales. Bruxelles 1899,—where references to the literature may be found.

† Pringsheims Jahrbücher für Wissenschaftliche Botanik 14, 27 (1884); there two other methods are described into which, however, we cannot enter more fully here. Zeitschr. f. physik. Chem. 2, 415 (1888); 3, 103 (1889).



independent of any accidental characteristics of the plant-cells employed.

*Tradescantia discolor* has cells that are especially well adapted to these purposes. The cuticle of the middle vein upon the under side of the leaf is employed.

Tangential sections are made of this, each of which contains several hundred living cells.

If these cells are placed in strong salt solutions, the protoplasmic contents shrink. Since the cell-wall does not alter its shape, the cell contents contract into a spherical mass, which usually remains connected with the cell-wall by a few strands, while the spaces intervening between the granular and at times pigmented protoplasm and the cell-wall are filled by the colourless, transparent, extravasated solution. (*C* in Fig. 26.) Since the protoplasm is surrounded by a membrane that is permeable for water, but

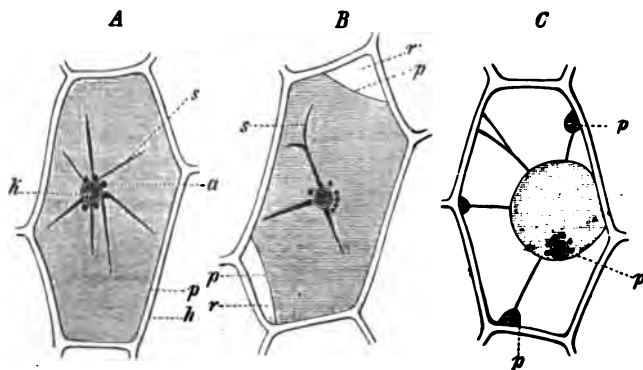


FIG. 26.

which prevents the passage of substances dissolved in the water, in case the salt solution into which the plant-tissue is dipped has a greater osmotic pressure than the proto-

plasmic contents, the latter will lose water and shrink. If the solution is less concentrated, then the shrinkage is correspondingly less, and the protoplasm then separates from the cell-wall only in the corners. (*B* in Fig. 26.) If the osmotic pressure of the solution is less than that of the cell-sap, or equal to it, then the protoplasm will not separate from the cell-wall. (*A* in Fig. 26.)

Now by finding the concentration of a solution in which plasmolysis occurs, and another, differing from it but slightly, in which plasmolysis does not occur, two limits are determined between which lies the concentration that is isotonic with that of the cell-sap.

If we find that plasmolysis occurs in a 1.01 per cent solution of potassium nitrate, and also in a 0.58 per cent solution of sodium chloride, while in a 1 per cent solution of potassium nitrate or a 0.57 per cent sodium chloride solution this does not occur, then the two first-named solutions are isotonic with the cell-sap, and consequently also with each other.

De Vries has employed the method of plasmolysis, amongst others, for determining the molecular weight of raffinose, concerning which various ideas were prevalent at the time. The molecular weight was given as:

$C_{12}H_{22}O_{11} + 3H_2O$  (= 396) by Berthelot and Ritthausen.

$C_{18}H_{32}O_{16} + 5H_2O$  (= 594) by Loiseau and Scheibler.

$C_{96}H_{64}O_{22} + 10H_2O$  (= 1188) by Tollens and Rischbiet.

By using cells from *Tradescantia discolor* de Vries determined the concentration of a raffinose solution that is isotonic with a cane-sugar solution containing  $\frac{1}{10}$  mol (=  $\frac{1}{10} \times 342$  g. = 3.42 per cent) per litre.

Experiment showed that a 5.96 per cent solution of raffinose has, at the same temperature, the same osmotic pressure as a 3.42 per cent solution of cane-sugar.

Since, according to the law of Avogadro-van't Hoff, the same number of molecules is present in solutions which at the same temperature have the same osmotic pressure, when  $x$  is the molecular weight of the raffinose sought, we can say:

$$\left. \begin{array}{l} \text{Number of molecules of} \\ \text{raffinose} \end{array} \right\} = \left\{ \begin{array}{l} \text{Number of molecules of} \\ \text{cane-sugar.} \end{array} \right.$$

$$\frac{3.42}{342} = \frac{5.96}{X},$$

or

$$X = 596.$$

This figure proves that the formula for raffinose originating with Loiseau and Scheibler,  $C_{18}H_{32}O_{16} + 5H_2O$ , is the correct one.

*b. The Determination of Osmotic Pressure by the Red-blood-corpuscle Method.*

This method, which originated with Hamburger,\* is based upon the following experiment: 20 c.c. of a 1.1 per cent potassium nitrate solution is put into a test-tube, and five drops of defibrinated beef-blood are added. The tube is then shaken, and the blood-corpuses are allowed to settle. After some time one sees a clear, almost colourless layer form above the blood-corpuses which is entirely free from red blood-corpuses or hæmoglobin.

Into a second test-tube are put 20 c.c. of a less concentrated potassium nitrate solution,—for example, one con-

\* Dubois-Reymonds Archiv, Physiologische Abt. 1886, 476; 1887, 31. Zeitschr. f. physik. Chem. 6, 319 (1890); Zeitschr. f. Biologie 26, 414 (1889). See also W. Löb, Zeitschr. f. physik. Chem. 14, 424 (1894). Willerding, Dissertation. Giessen 1897.

taining 1.0 per cent of the salt; to this are also added five drops of the same blood. The blood-corpuscles settle here also, only the supernatant fluid is no longer colourless, but is tinged with red,—the blood-corpuscles have lost some of their colouring matter.

If now two limits of concentration, not only for saltpetre but also for other substances and for sugar, are sought, one in which the blood-corpuscles sink and leave behind a colourless solution, and a second in which the liquid left behind shows a red colour, we find that the solutions the concentrations of which are represented by the average between these two concentration limits are isotonic. The following table contains a summary of the results obtained. The accuracy that can be attained is greater than is apparent from the table; for a potassium nitrate solution containing 0.97 per cent of the salt can be clearly distinguished from one containing 0.96 per cent.

If now we know that a certain solution, at a certain temperature, is isotonic with a sugar solution of a known concentration, then we know the osmotic pressure of the solution, for the osmotic pressure of the sugar solution can be calculated from the law of Avogadro-van't Hoff.

Name of substance.	Concentration of the solution in which the blood-corpuscles do not lose their colouring matter.	Concentration of the solution in which the blood-corpuscles begin to lose their colouring matter.	Average concentration.
Potassium nitrate ...	1.04%	0.96%	1.00%
Sodium chloride....	0.60	0.56	0.58
Cane-sugar.....	6.29	5.63	5.13
Potassium iodide....	1.71	1.57	1.64
Sodium iodide.....	1.54	1.47	1.55
Potassium bromide..	1.22	1.13	1.17
Sodium bromide.....	1.06	0.98	1.02

In the last column of this table are given the concentrations of the solutions of the various substances in which the blood-corpuscles do not lose their colouring matter. These solutions are therefore isotonic with each other.

According to the law of Avogadro-van't Hoff, since these solutions are isotonic, they should contain an equal number of dissolved molecules at the same temperature—that is, they should be equimolecular. The following summary shows that this is indeed the case:

One litre of the  $\text{KNO}_3$  solution contains 10.00 g.  $\text{KNO}_3$  per litre, therefore  $\frac{10}{101} = \frac{1}{10}$  mol.

One litre of the  $\text{NaCl}$  solution contains 5.85 g.  $\text{NaCl}$  per litre, therefore  $\frac{5.85}{58.5} = \frac{1}{10}$  mol.

One litre of the  $\text{KI}$  solution contains 16.4 g.  $\text{KI}$  per litre, therefore  $\frac{16.4}{166} = \frac{1}{10}$  mol.

One litre of the  $\text{KBr}$  solution contains 11.7 g.  $\text{KBr}$  per litre, therefore  $\frac{11.7}{119} = \frac{1}{10}$  mol.

Equimolecular solutions of different substances consequently show the same behaviour toward red blood-corpuscles, just as is the case, according to the experiments of de Vries (see p. 145), in their effect upon plant-cells.

If in using the red blood-corpuscles of cattle it is found that two solutions are isotonic, then this isotonicity is also found to exist when the blood-corpuscles of other animals are used. Yet it must be remembered that the concentrations of the solutions at which the hæmoglobin is first extruded may vary greatly with the different kinds of blood-corpuscles. Thus the colouring matter of the corpuscles of the frog is extruded in a sodium chloride solution when the concentration of the salt amounts to 0.21 per cent; from the blood-corpuscles of man the hæmoglobin is ex-

truded at a concentration of 0.47 per cent; from those of the chicken at 0.44 per cent.

Solutions in which the colouring matter is extruded do not have the same osmotic pressure as the blood-corpusele contents, but a lower one, for otherwise the red blood-corpuseles would not have increased in volume in them. Because of this increase they finally burst and allow a part of their colouring matter to dissolve in the solution.

The concentrations of the solutions that are isotonic with the blood-corpusele contents could be found by determining the concentrations of the solutions in which no change in the volume of the corpuseles occurs.

I would here like to speak briefly of the expression "physiological salt solution," an expression which, though in daily use, has given rise to much confusion, as Hamburger\* and Köppe† have pointed out. Very often we find this name applied to a 0.6 per cent sodium chloride solution, yet we find very diverse reasons given for this fact. This name has arisen from the idea that such a solution conducts itself entirely indifferently toward animal tissues. This, now, is by no means the case, and holds good, and then but approximately, only for the blood-corpuseles of the frog. The blood-corpuseles of men, horses, and cattle increase in volume very considerably in such a solution, while in a 0.9 per cent sodium chloride solution no change in volume occurs. This name might then be applied in the above sense much more properly to the latter solution. Still this name has no general significance, for

\* *La Flandre médicale* 1894; cited from a reprint. *Maandblad voor Natuurwetenschappen* 19, 102 (1895). See also Jacques Loeb, *Pflügers Archiv* 69, 15 (1898).

† *Pflügers Archiv* 65, 492 (1897).

this concentration would again have to be altered in dealing with other animal tissues. For this reason it is more in harmony with our modern ideas when we indicate in each case the osmotic pressure of the salt solution which causes no change in the given tissue, and so entirely do away with the expression "physiological salt solution."

According to Hamburger's experiments the serum of many animals is isotonic with a 0.9 per cent sodium chloride solution; solutions the osmotic pressure of which (at the same temperature) is higher than that of this sodium chloride solution we shall with Hamburger term *hyperisotonic*, those the osmotic pressure of which is lower *hypisotonic*.

*c. The Determination of Osmotic Pressure by the Hæmatocrit.*

At the suggestion of C. Eijkman a method for determining isosmotic concentrations was worked out by Grijns,\* and shortly thereafter by Hedin,† which was later employed also by Köppe ‡ in the study of many important problems. The apparatus has retained the name given it by Hedin, *hæmatocrit*.

This method depends upon the fact that red blood-corpuscles change their volume when they are brought into a

\* Verslagen Kon. Akad. v. Wetenschappen te Amsterdam, Februari 1894; Geneeskundig Tijdschrift voor Ned. Indië 35, Afl. 4; Jaarverslag van het Laboratorium voor pathologische Anatomie en Bakteriologie te Weltevreden 1894; Pflügers Archiv 63, 86 (1896).

† Skandinavisches Archiv für Physiologie 2, 134 and 360; *ibid.* 5, 207, 238, 277; Zeitschr. f. physik. Chem. 17, 164 (1895). Pflügers Archiv 60, 360 (1895).

‡ Dubois-Reymonds Archiv, Physiol. Abt. 1894, 154. Zeitschr. f. physik. Chem. 16, 261 (1895); Münchener mediz. Wochenschrift 1893, 24.

solution the osmotic pressure of which differs from that of their contents.

In solutions the osmotic pressure of which is greater than that of the cell contents, the volume of the cells is diminished in that water is extracted from them. The converse also holds. Solutions in which the blood-corpuscles undergo no change in volume must according to this be isotonic with each other. If we remember that the change in volume is determined by the difference between the osmotic pressure of the given solution and that of the blood-corpuscle contents, then we can also say that two solutions in which the change in the volume of the blood-corpuscle is the same are isotonic. Now these changes in the volume of the

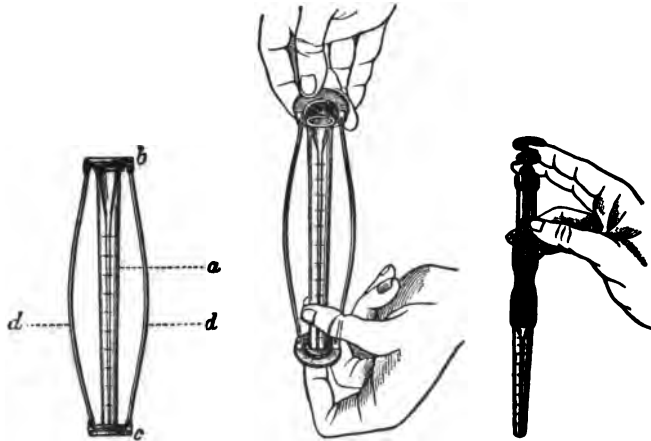


FIG. 27.

blood-corpuscles in different solutions can be measured by the hæmatocrit.

The form given the apparatus by Köppe is illustrated in Fig. 27.



*a* is a pipette 7 cm. long, made of thermometer tubing and graduated into 100 parts; *b* and *c* are two metal plates that serve as seals which can be clamped against the openings of the pipette by means of the bent rods *dd*. In order to make the closure of the openings perfect, the plates are covered with rubber, while the lower plate in addition carries a cork disc.

When the pipette is to be used, it is connected with a Pravaz syringe. From a drop of blood obtained by pricking the tip of the finger, blood is drawn into the pipette to any definite mark by slightly raising the plunger. The point of the pipette is cleansed of adhering blood, and the given salt solution is immediately sucked in after the blood. The two mix in the funnel-shaped part of the apparatus. The left hand now presses the lower of the two seals against the point of the pipette, while the right hand removes the syringe, mixes the blood and salt solution with a clean needle, and seals the pipette.

After enclosing in a small wooden shell, the pipette is fastened into a centrifuge and centrifuged. The blood-corpuses collect at the periphery and form a red column in the tube, which at first diminishes uniformly in size, but finally becomes constant. The centrifuging must be kept up until this point is reached. From the length of the column of blood drawn in and the length of the column of blood-corpuses it can be determined what per cent of the entire volume is occupied by the blood-corpuses.

If, for example, the blood has been drawn into the pipette to the *n*th mark, and the blood-corpuse column stands at the *m*th mark, then the volume of the latter is

$$\frac{100}{n}m \text{ per cent.}$$

We will illustrate the use of the hæmatocrit by giving an example.

Suppose we wish to determine the concentration of a potassium nitrate solution which is (at the same temperature) isotonic with a sugar solution containing 0.2 mol sugar per litre.

We first of all centrifuge the blood with the given sugar solution in the manner described, and determine the volume of the blood-corpusele column.

Sugar solution 0.2 mol per litre:	
Blood column.....	100
Blood-corpusele column.....	58.5
	58.5
Volume of corpuscles in per cent.....	58.5

We then examine several potassium nitrate solutions having different concentrations in the same manner:

KNO <sub>3</sub> solution 0.125 mol per litre:	
Blood column.....	99
Blood-corpusele column .....	53.5
	54.0
Volume of corpuscles in per cent.....	54.0
KNO <sub>3</sub> solution 0.1 mol per litre:	
Blood column.....	100
Blood-corpusele column.....	60.0
	60.0
Volume of corpuscles in per cent.....	60.0

While, therefore, a potassium nitrate solution containing 0.125 mol per litre gives the figure 54 in the hæmatocrit, one that contains 0.1 mol yields the figure 60.0, while the sugar solution gives 58.5. There is now to be determined what potassium nitrate solution will give the figure 58.5, for such a solution is isotonic with the sugar solution.

Since 6 divisions (60 - 54) in the pipette scale correspond to the change in concentration from 0.125 to 0.100, 4.5

divisions (58.5–54) on the scale will correspond with one of  $\frac{4.5}{6} 0.025 = 0.0197$ . The concentration of the saltpetre solution sought, which is isotonic with the sugar solution, will consequently be  $0.125 - 0.019 = 0.106$  mol  $\text{KNO}_3$  per litre.\*

If the temperature at which the measurement has been made is known, we can calculate the osmotic pressure of the sugar solution (containing 0.2 mol per litre) used, by the law of Avogadro-van't Hoff, and so know also the osmotic pressure of the potassium nitrate solution in atmospheres.

*d. The Determination of Osmotic Pressure by Other Physiological Methods.*

I would also like to direct your attention to the investigations of Massart.† This observer, by means of a glass capillary, introduced some potassium carbonate solution into a drop of bouillon in which bacteria had been grown.

The potassium carbonate serves to attract the bacteria; the bacteria enter the capillary tube, and after twenty to thirty minutes this is entirely filled with them. If, however, increasing amounts of a salt (for example, sodium chloride) are added to the carbonate solution, it is found that the bacteria enter only into the weakest solutions, while they are repelled by the stronger ones. Now it is possible to find a solution the use of which causes the bac-

\* We shall later explain why a sugar solution containing 0.2 mol sugar per litre is not isotonic with a potassium nitrate solution containing 0.2 mol  $\text{KNO}_3$  per litre.

† Archives de Biologie Belges 9, 15 (1889), where references to the literature may be found.

teria to collect at the entrance of the capillary without entering it.

In Massart's experiments it was found that *Spirillum undula* and *Bacillus megatherium* enter the solutions of very different salts when the concentration of these salts is equal to 0.04 mol per litre (or less); if the concentration is 0.05 mol per litre, they remain at the entrance of the capillary. One receives the impression that the organisms, as soon as the loss of water which they suffer in the stronger solutions makes itself felt, leave the place that threatens their existence.

Here also equimolecular solutions produce similar effects.

Massart's studies into the sensitiveness of the eye toward salt solutions of various concentrations are also interesting.

As is known to you, the introduction of pure water into the eye calls forth an unpleasant sensation. This is also the case when a concentrated salt solution is brought under the eyelids. Between these two concentrations it is possible to find one which, like the tears, is non-irritable. It was found that such a solution is isotonic with the tears. In this way, therefore, use can be made of the sensitiveness of the eye to establish the isotonicity of different solutions. Massart found that a sodium chloride solution containing 1.39 per cent \* of the salt is isotonic with the tears. According to the chemical analysis of Beaumis,†

\* As we shall see later, the albuminoids dissolved in the tears cannot influence the osmotic properties of this fluid, because of their high molecular weight, and may therefore be neglected here.

† Besides NaCl only very slight amounts of other salts are dissolved in the tears.

1.3 per cent NaCl is present in the tears, which harmonises well with Massart's findings.

Finally, the observations of Wladimiroff \* must be mentioned, who established the isotonicity of different solutions by determining the concentrations at which certain bacteria cease their movements in them.

#### DIFFUSION.

It has already been pointed out (p. 135) that when the concentration of the dissolved substance is not the same at all points in a solution, the substance moves from places of higher concentration to those of lower, and that this movement is termed *diffusion*.

With gases similar phenomena occur. If, for example, we introduce bromine into a vessel filled with a gas, such as air, we see that the brownish-red bromine vapour gradually spreads through the entire mass of gas, and that this movement does not cease until the bromine has distributed itself uniformly throughout the entire space. Here also an equalisation of the concentration is brought about through diffusion (gas diffusion).

If the pressure of the bromine at a certain place is  $P$ , while at another place it is lower,  $p$ , then the cause of the diffusion is to be attributed to the existence of the difference in pressure  $P - p$ , and the velocity with which the bromine particles migrate is proportional to this difference in pressure.

In an entirely analogous way diffusion in liquids is determined by the osmotic pressure of the dissolved substance.

If at two places in a solution the concentrations of the

\* Archiv f. Hygiene 10, 81 (1891); Zeitschr. f. physik Chem 7, 521 (1891).

dissolved substance are different, then this difference in concentration, as we have seen above, corresponds to a difference in osmotic pressure between the given points, and a movement of the dissolved substance must therefore occur from the place of higher osmotic pressure to that of lower osmotic pressure. The driving force is here the difference between the two osmotic pressures, and the diffusion velocity will be proportional to this difference in pressure.

The first thorough investigations of diffusion in liquids date from Graham \* (1851), yet not until 1855 was a law formulated by Fick † embracing the phenomena of diffusion. This can now, since the osmotic pressure of the dissolved substance has been recognised by Nernst ‡ to be the cause of the diffusion, be stated as follows:

The amount of the dissolved substance that in the unit of time diffuses through a given cross-section of a liquid is proportional to the difference in the osmotic pressure which exists between two cross-sections that lie very (infinitely) near each other.

To form a conception of the idea *diffusion coefficient*, let us imagine a cylindrical mass of a solution (Fig. 28). The cylinder has a length of 1 cm. and a cross-section of 1 sq. cm. Between the concentration of the solution in the area *A* and that in *B* exists the difference in concentration 1, and care is taken that this difference exists always.

The dissolved substance will now move (in the direction

\* *Annalen der Chemie und Pharmacie* 77, 56 and 129 (1851); 80, 197 (1851); 121, 1 (1862). Marignac, *Annales de Chimie et de Physique* (5) 2, 546 (1874). Liebermann and Bugarszky, *Zeitschr. f. physik. Chem.* 12, 188 (1893) Höber, *Pflugers Archiv* 74, 225 (1899).

† *Poggendorffs Annalen* 94, 59 (1855).

‡ *Zeitschr. f. physik. Chem.* 2, 613 (1888).

of the arrow) toward the side of lowest concentration (*B*). Now the amount of dissolved substance which, when constant conditions are established in the cylinder, diffuses through the cylinder in the unit of time, is termed the *diffu-*

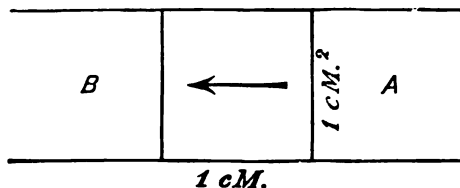


FIG. 28.

*sion coefficient* of the dissolved substance at the temperature at which the determination is made.

The day is chosen as the unit of time, since diffusion takes place so slowly that if a smaller unit of time were chosen the amount of substance that would diffuse would be very small. When we say that the diffusion coefficient of urea at  $7.5^\circ$  is 0.810, we mean that at the given temperature 0.810 g. of urea diffuse per day from a one per cent urea solution through a cylinder 1 cm. long and 1 sq. cm. in diameter. How now can we determine this diffusion coefficient experimentally?

Scheffer\* proceeded as follows:

A bottle *E* (Fig. 29) holding about 90 c.c. and cylindrical at its lower end (4 cm. wide, 6.5 cm. high) is closed with a ground stopper *B*. The neck of the bottle is about 1.5 cm. in diameter. Through the stopper passes a narrow tube (11 cm. long, 0.5 mm. in diameter) carrying

\* Ber. d. deutsch. chem. Gesellsch. 15, 788 (1882); 16, 1903 (1883)  
Zeitschr. f. physik. Chem. 2, 390 (1888).

the stop-cock *F* and the globe *D*. The latter holds about 16 c.c. between the marks *S*<sub>1</sub> and *S*<sub>2</sub>. The tube ends just above the bottom of the bottle. The slightly bent tube *C* is fused to the stopper *B*. If, for example, the diffusion coefficient of urea is to be determined, water is introduced into the bottle (three times the volume of the pipette *D*) and the pipette, filled with the given urea solution, is set into place. The whole apparatus is then put into a room the temperature of which is kept as nearly constant as possible. For since the diffusion coefficient is a function of the temperature, and increases about 2 per cent for each degree of temperature increase, this point is of great importance. But besides this, through local variations in temperature, currents might be produced which would disturb the process of diffusion. It is for these reasons and because of the difficulty of entirely avoiding vibrations of the apparatus during the experiment, that diffusion measurements belong among the most difficult determinations made in the field of physical chemistry.

When a constant temperature has been established, the stop-cock *F* is opened and, to avoid mixing with the water in *E*, the solution is permitted to flow very slowly into the bottle. When the solution has flowed out to the mark *S* the stop-cock is closed.

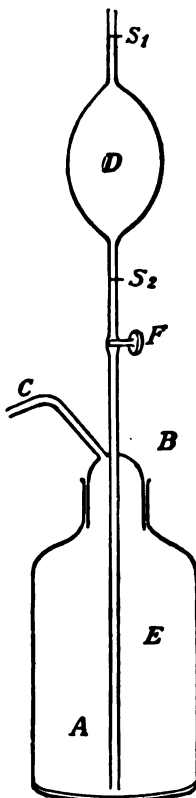


FIG. 29.



When the experiment is to be ended in order to determine the amount of dissolved substance that has diffused, the pipette is again filled with urea solution. This is permitted to flow into the bottle by opening the stop-cock, until the liquid in *E* has reached the tube *C*. The pipette is then again filled and emptied into *E*, while the liquid flowing from *C* is received into a flask and set aside for analysis.

These manipulations are repeated in such a way that the contents of the bottle are obtained in four different portions, which are analysed separately. By this means are determined the amounts of dissolved substance that have diffused after a definite time into the various layers of the liquid.

We cannot here enter into a discussion of the somewhat complicated calculation of the diffusion coefficients from the data derived from the analyses. The following figures are given as examples:

Diffusing substance.	Temperature.	Diffusion coefficient.
Urea.....	7.5°	0.81
Chloral hydrate .....	9.0	0.55
Mannite.....	10.0	0.38

We have already discussed the meaning of the values given in the last column. So far as the diffusion of the strong acids, bases, and salts is concerned, we can here only say that with the help of the diffusion theory of Nernst, which is based upon the theory of osmotic pressure, it is possible to calculate in advance the diffusion coefficients of these substances.

In how far this theory harmonises with the results obtained by experiment is shown in the following table, in which *k* represents the diffusion coefficient of the given substance at 9°.

In judging of this agreement we must remember what has been said above: diffusion determinations are to be counted among the most difficult problems of experimental physical chemistry.

Name of substance.	$k$ (observed).	$k$ (calculated).
Hydrochloric acid.....	2.30	2.35
Potassium hydroxide .....	1.85	2.13
Sodium chloride.....	1.11	1.19
Sodium nitrate.....	1.03	1.15
Sodium acetate.....	0.78	0.86

While gases diffuse with great rapidity,—one has but to remember the great rapidity with which odorous substances spread to great distances,—the diffusion velocity of dissolved substances is, as the above figures indicate, exceedingly low.

This is to be attributed to the fact that a dissolved substance in its movement through a liquid has to overcome an enormous friction. An analogue is to be found in the great slowness with which fine powders suspended in a liquid settle to the bottom, even though they have a greater specific gravity than the liquid in which they are found.

By means of Nernst's theory of diffusion, the force necessary to move one mol of cane-sugar (342 g.) through water with a velocity of one centimetre per second is calculated to be 6700 million kilograms; this force is a measure of the enormous resistance that the sugar molecules have to overcome in diffusion.

We have up to this point described the phenomena of diffusion only in their simplest form, that is to say, when diffusion occurs without an intervening membrane. From a physiological point of view, the latter case is of great

importance; for in plants and animals diffusion often takes place between solutions that are separated by membranes which permit the dissolved substances to pass through only in part.

The influence which such membranes exert upon the phenomena of diffusion (or the velocity of absorption in the animal body) has recently been the subject of extensive investigation, yet a discussion of this question must be omitted here, since the subject has not yet been definitely settled.\*

Of great importance to the physiologist is the fact established by Graham † and Voigtländer ‡ that the diffusion velocity of dissolved substances is not altered when gelatinous substances, such as glue, agar-agar, etc., are added to the liquid in which the diffusion takes place; even the addition of 4 per cent agar-agar to an aqueous solution does not alter the diffusion velocity.

This fact is also of importance in the study of the phenomena of diffusion, for the errors which so easily creep into diffusion determinations in consequence of the slightest vibration of the apparatus can be entirely done away with through the addition of agar-agar to the solution.

We have already pointed out (see p. 32) that reaction velocity is not influenced by the presence of gelatinous

\* Hamburger, Dubois-Reymonds Archiv, *Physiol. Abt.* 1896, 302 and 438. Cohnheim, *Zeitschr. f. Biol.* 18, 129 (1898). Höber, *Pflügers Archiv* 74, 225 and 246 (1899), where references to the literature may be found. Hedin, *ibid.* 78, 205 (1899). Kövesi, *Physiol. Centralblatt* 11, 595. Eckardt, *Über die Diffusion und ihre Beziehung zur Giftwirkung. Dissertation. Leipzig* 1898. Overton, *Zeitschr. f. physik. Chem.* 22, 189 (1897).

† Liebig's *Annalen der Chemie und Pharmacie* 121, 1 (1862).

‡ *Zeitschr. f. physik. Chem.* 3, 316 (1889). See also Arrhenius, *ibid.* 10, 51 (1892).

substances. The catalysis of methyl acetate, as we have already seen, proceeds with the same velocity in an agar-agar jelly as in water. This fact harmonises with what has just been said concerning diffusion velocity in such media. For in order that a reaction may ensue between the molecules of different substances the molecules must move through the medium in which they are dissolved. If this medium has no influence upon the velocity of their movement, then it can also have no influence upon their meeting in the solution.

I would also like to return for a moment to the so-called *solid solutions* which were briefly mentioned above (see p. 118), for there are a number of facts in the field of diffusion which prove the existence of such solutions.\*

If, at ordinary temperature, a lead cylinder is set upon a cylinder of gold, and the two are pressed against each other by means of screws, the gold diffuses into the lead. This fact can be tested by cutting thin sections from the lead cylinder from time to time, and examining them for the amount of gold they contain. Roberts-Austen used for such experiments cylinders 0.28 cm. in diameter and 25 cm. high. After four years the lead and gold cylinders were entirely fused together. A lead disc was cut out of the cylinder at a height of 0.75 mm., and several others at a height of 0.23 mm. In the four lower discs the presence of gold was clearly demonstrable, in the succeeding sections only in traces.

When the influence of temperature upon these phenom-

\* Spring, *Zeitschr. f. physik. Chem.* 2, 536 (1888); *ibid* 15, 65 (1894). Roberts-Austen, *Philosophical Transactions of the Royal Society* 187, 383 (1896). Also, *Proceedings of the Royal Society* 67, 101 (1900).

ena of diffusion was investigated it was found that the amount of gold which diffuses at 18° into solid lead would be the same after 1000 years as that which diffuses into molten lead (272° C.) in one day.

In conclusion I wish to say a few words concerning *colloids* \* and *crystalloids*.

Graham already in his fundamental publications † pointed out that there are a number of substances which, in contrast to the strong mineral acids, bases, and salts, diffuse very slowly. The rapidly diffusing substances are mostly crystalline, while the slowly diffusing ones are amorphous.

The latter he called *colloids* (because glue belongs to this group), the former *crystalloids*.

In the light of the theory of osmotic pressure this behaviour of the colloids becomes at once intelligible. The slow diffusion corresponds to a low osmotic pressure, and it is indeed found that this pressure is exceedingly low in the case of the substances named, since they have a high molecular weight. So, for example, from Pfeffer's measurements of the osmotic pressure of solutions of glue, its molecular weight is calculated to be about 5000; from Linebarger's measurements the molecular weight of the colloidal tungstic acid is calculated to be about 1700.

While crystalloids diffuse uninterruptedly through colloidal membranes, such as agar-agar, animal bladders, etc., colloidal solutions cannot pass through them. Upon these phenomena rests the familiar fact that crystalloids

\* See references to the literature in A. Lottemoser, Die anorganischen Kolloide, Stuttgart 1901.

† See foot-note p. 164.

can be separated from colloids by using animal membranes or parchment paper (dialysis).

No sharp border-line, however, exists between colloids and crystalloids; this is evidenced by the fact that the diffusion of many crystalloids is also hindered by colloidal membranes.\*

\* The communication of C. Eijkman, which has just appeared (*Centralbl. f. Bacteriologie, Parasitenkunde und Infektionskrankheiten* 29, 841, 1901), according to which a solution of glue poured upon an agar-agar plate diffuses into the agar-agar in a short time, if only care be taken to maintain a suitable temperature so that the solution does not coagulate, is very worthy of note. Eijkman believes to have proved hereby that colloids can also diffuse into colloids. Further investigations in this direction might prove fruitful.

## TENTH LECTURE.

### The Determination of the Molecular Weight of Dissolved Substances.

#### *a. The Depression of the Freezing-point.*

WE have already shown (see p. 147) how the indirect measurement of the osmotic pressure by the method of plasmolysis may be used to determine the molecular weight of a dissolved substance.

A direct measurement would be preferable to this, yet we possess, as has been said, up to this time no method which permits of a direct measurement of osmotic pressure with exactness.

We shall now direct our attention to two methods which again indirectly, with greater accuracy however than by biological means, enable us to determine the molecular weight of dissolved, non-volatile substances.

The English military surgeon Blagden \* observed as early as 1788 that the freezing-point of a solution is lower than that of the pure solvent.

Since in ascertaining the depression of the freezing-point (*cryoscopy*) of dilute solutions we deal mostly with the determination of slight differences in temperature, special contrivances for such measurements are in use.

The apparatus of Beckmann † is often used for such

\* Philosophical Transactions of the Royal Society 78, 277 (1788).  
Ostwalds Klassiker der exakten Wissenschaften No. 56 (1894).

† Zeitschr. f. physik. Chem. 2, 638 (1888); 7, 323 (1891); 21, 239 (1896). The method of determining the depression of the freezing-

purposes. This is illustrated in Fig. 30. *C* is a battery-jar carrying a metal cover. Through an opening in the cover is pushed the glass tube *B*, into which is fixed a perforated cork. Through the perforation passes the freezing-vessel *A*, carrying a side tube to facilitate the introduction of the substance to be examined. The space between *A* and *B* serves as an air-jacket; this air-jacket allows any solution introduced into *A* to assume only gradually the temperature of its surroundings (in *C*). The freezing-vessel is closed with a cork, through which pass a thermometer *D* and a stirrer of platinum wire. The thermometer is graduated into hundredths of a degree; the thousandth part of a degree can be estimated.

If with such an apparatus the depression of the freezing-point of a sugar solution is to be determined, we proceed as follows:

Into *A* is introduced a weighed amount of distilled water,\* and the thermometer, the bulb of which is entirely submerged, is put into place.

point is, among other things, fully described in H. Biltz, *Die Praxis der Molekelgewichtsbestimmung*. Berlin 1898.

\* The state of purity demanded by this water will be set forth

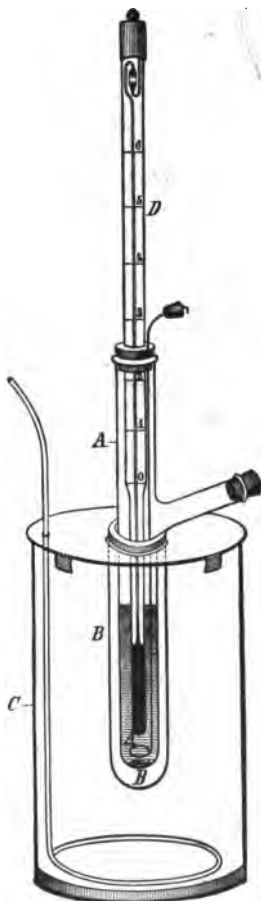


FIG. 30.



The cylinder *C* is filled with a freezing-mixture of a *constant* temperature, lying a few tenths of a degree below the probable freezing-point of the solution. We shall return later to this freezing-mixture.

The freezing-tube is next cooled by thrusting it into the freezing-mixture. When the temperature of the water in *A* has approached the freezing temperature, *A* is set into *B*, and *B* into *C*. The temperature of the water now slowly drops, even to below the freezing-point (*undercooling*).

When an undercooling of several tenths of a degree has been reached, the water is vigorously stirred with the stirrer. Usually the water freezes at once; should this not happen, a very small crystal of ice is introduced into the tube *A*. The thermometer now suddenly rises, since in freezing the latent heat of fusion of the water is liberated. Finally the temperature reaches a maximum, which lasts for several minutes. This temperature is read from the thermometer and noted as the freezing temperature of the water. The tube *A* is then held in the hand in order to melt the ice that has formed, and a weighed amount of sugar is introduced into the water through the side tubulation. It is very convenient to let the substance to be dissolved slide through the side neck into the freezing-vessel in the form of a pastille. These pastilles can be prepared in a small press especially arranged for this purpose. After the solution has been thoroughly mixed by stirring, the manipulations which have just been described for pure water are repeated, and the freezing-point of the given solution found in this way.

By subtraction is obtained the depression which the in greater detail later, in considering the conductivity of dissolved electrolytes.

freezing-point of the water has suffered by dissolving the sugar in it. A few remarks concerning the conditions under which a freezing-point determination must be made may not be out of place.

Of great importance is the regulation of the temperature of the freezing-mixture. Up to a few years ago, the majority of such determinations were made with great undercooling, that is to say, the freezing-mixture used had a temperature which lay many degrees below that of the freezing temperature of the solution. The observations of Nernst and Abegg,\* into which we cannot enter here, have shown, however, that through the use of such great undercooling important errors creep into the determination of the freezing-points of the solutions. Care is therefore to be taken to select a freezing-mixture the temperature of which lies not more than a few tenths of a degree below the freezing-point of the solution.

These constant temperatures can be obtained by making use of the so-called *cryohydrates*.† For this purpose a

\* *Zeitschr. f. physik. Chem.* 15, 681 (1894). See also Raoult, *ibid.* 27, 617 (1898), where references to the literature may be found; Battelli and Stefanini, *Nuovo Cimento* (4) 9, 1899. Cited from a reprint.

† To illustrate the term "cryohydrate," the following may be said: If a salt solution is cooled, pure ice begins to form, when the freezing-point of the solution is reached. The concentration of the solution is in consequence increased; if the remaining solution is still further cooled, a temperature is finally reached at which the solution is saturated. Upon further lowering the temperature a mechanical mixture of ice and salt separates out, in which the two exist in the same proportion as in the saturated solution. At this temperature the mixture of ice and salt, called a *cryohydrate*, melts at an absolutely constant temperature. As long as the entire mass has not become liquid the temperature remains constant during the process of melting. See E. Schrader, *Programm des Realgymnasiums zu Insterburg* (1889), where references to the litera-

mixture of a finely powdered salt and ice or salt and snow is introduced into the cylinder *C*, care being taken that an excess of salt is always present. In the following short table are given the constant temperatures that may be obtained by using the salts indicated:

Name of salt.	Temperature.	Name of salt.	Temperature.
Potassium alum . . . . .	-0.4°	Potassium nitrate . . . . .	-3°
Glauber's salt . . . . .	-0.7	Zinc sulphate . . . . .	-5
Potassium bichromate	-1	Strontium nitrate . . . . .	-6
Potassium sulphate . . . . .	-1.5	Barium chloride . . . . .	-7
Copper sulphate . . . . .	-2		

Instead of these cryohydrates, for the maintenance of constant temperatures, the cold bath may be used with advantage, the temperature of which is kept constant through the evaporation of sulphuric ether or carbon bisulphide. The apparatus used for this purpose (Fig. 31) is that employed by Claude and Balthazard\* for determining the freezing-point of urine, and is modelled after that of Raoult.† The results obtained with this instrument are very satisfactory, for which reason it might recommend itself as a clinical instrument. *a* is the freezing-vessel, *b* an outer vessel to protect *a*, which is similar to that found in the Beckmann apparatus. Into the cylinder *A* is put ether (three-fourths full), into *b* alcohol to serve as a conductor between the ether and the liquid in the freezing-glass. The surface of the alcohol in *b* is always to be below that of the liquid in *a*.

ture are to be found. Also, Pfaundler, Bericht. d. d. Chem. Ges. 10, 2223 (1877). Offer, Wiener Akad. Berichte (2) 81, 1058 (1880). Roloff, Zeitschr. f. physik. Chem. 17, 325 (1895). de Coppet, *ibid.* 22, 239 (1897).

\* La Cryoscopie des Urines, Paris 1901.

† Zeitschr. f. physik. Chem. 27, 617 (1898).

The tube *c* is connected with an hydraulic air-pump; when this is in operation, air passes by way of the bottle *B*, in which is contained some sulphuric acid for drying purposes, through a number of holes into the ether and causes

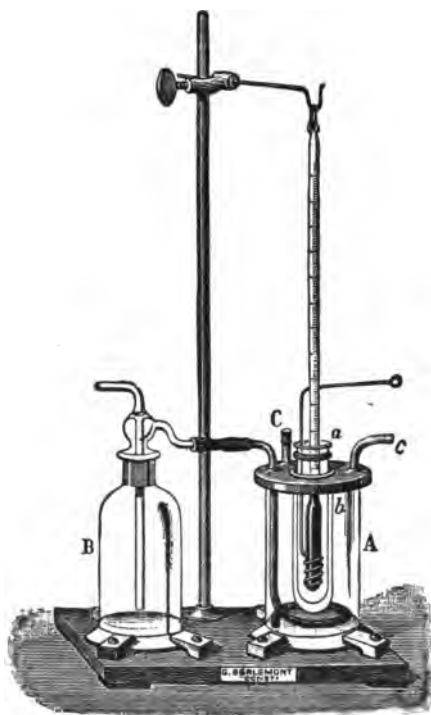


FIG. 31.

this to evaporate rapidly. The temperature can be regulated or kept constant in a most convenient way by regulating the current of air. Further than this the determinations are to be made as with the Beckmann apparatus.

If the freezing-points of solutions of various substances

are determined in the manner described, it is found, as Blagden had already observed, that the depression of the freezing-point is proportional to the concentration of the dissolved substance.

The following table shows this for aqueous solutions of sugar. Under  $m$  is given the number of mols of sugar per 100 g. of water, under  $t$  the depression of the freezing-point observed. Further than this the value  $\frac{t}{m}$  has been calculated, that is, therefore, the (theoretical) depression of the freezing-point that a solution would show in case one mol of the dissolved substance were present in each 100 g. of the same. The latter figure ( $K$ ) is designated the *molecular depression of the freezing-point*.

$m$	$t$	$K$
0.01305	0.2450	18.8
0.00688	0.1247	18.1
0.003534	0.0634	17.9
0.00178	0.0337	18.8

If, in a similar manner, we determine for other substances, such as urea, ethyl alcohol, etc., the depression of the freezing-point which they would cause in case one mol of the same were dissolved in 100 g. of water, the same value is found for  $K$ . So, for example, for an aqueous solution of ethyl alcohol there was found:

$m$	$t$	$K$
0.01324	0.2432	18.4
0.00705	0.1307	18.5
0.00364	0.0685	18.8

As an average of many determinations made with the aqueous solutions of very different substances,  $K$  has been found to equal 18.6. This figure indicates that in case

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one mol of any substance \* is dissolved in 100 g. of water, the freezing-point of this solution is depressed 18.6°, that is to say, it freezes at -18.6° instead of at 0° (the freezing-point of the water). Now, for every solvent, a definite value may in this way be found for the molecular depression (*K*) of the freezing-point.

The following table gives this value for several solvents, as also their freezing-points (melting-points):

	Water.	Acetic acid.	Benzene.
Molecular depression of the freezing-point <i>K</i> . . . . .	18.6°	39.0°	49.0°
Freezing-point . . . . .	0	16.7	5.4

If now the molecular weight of a substance soluble in any given liquid is unknown, but the value of *K* for this solvent is known, it is possible, by determining the depression of the freezing-point of a solution containing a known amount of the substance, to determine the molecular weight of this substance.

If *A* represents the experimentally determined depression of the freezing-point which 100 g. of the solvent suffers through the addition of *p* grams of substance, *K* the molecular depression of the solvent, and *M* the molecular weight of the substance to be determined, then, since in 100 g. of the solvent  $\frac{p}{M}$  mols of dissolved substance are present, and one mol of dissolved substance in 100 g. of solvent produces a depression of the freezing-point of *K* degrees:

$$A : K = \frac{p}{M} : 1,$$

wherefore

$$M = \frac{Kp}{A}. \quad (1)$$

The following experiments are given as examples:

a. The depression of the freezing-point of a cane-sugar solution

\* We shall return later to the exceptions to this rule in the discussion of electrolytic dissociation.

containing 4.4631 g. of sugar in 100 g. of water was determined in a Beckmann apparatus. The freezing-point was found to be  $0.2450^{\circ}$ . According to this the molecular weight of the cane-sugar is

$$M = \frac{18.6 \times 4.4631}{0.2450} = 338.8.$$

The formula  $C_{12}H_{22}O_{11}$  gives 342.

b. The depression of the freezing-point  $d$  of a solution containing 4.47 g. of acetic acid in 100 g. benzene was found to be  $1.790^{\circ}$ .  $K$  for benzene equals  $49^{\circ}$ . If these known values are substituted for the unknown in equation (1), we find

$$M = \frac{49 \times 4.47}{1.790} = 123.$$

Now upon chemical grounds the formula of acetic acid has been found to be  $CH_3COOH$ ; this formula gives 60 for the molecular weight. Since upon cryoscopic grounds we have found 123, this is a proof for the assumption that in the benzene the molecules of acetic acid unite into double molecules—*association* takes place.

If the molecular weight ( $M$ ) of a dissolved substance is known, and the freezing-point ( $d$ ) of a solution containing  $p$  grams of substance in 100 g. of the solvent has been determined, then the molecular depression of the solvent can be calculated from equation (1); for it is

$$K = \frac{Md}{p}.$$

Until now we have considered the molecular depression ( $K$ ) as a value to be determined experimentally for each solvent. The extensive investigations of Raoult \* at first showed such to be indeed the case.

Most important, however, is the fact that these constants, as van't Hoff † has shown, can be *calculated* from other values.

\* Annales de chimie et de physique (5) 28, 137 (1833); (6) 2, 66 (1884).

† Zeitschr. f. physik. Chem. 1, 481 (1887) and Ostwalds Klassiker der exakten Wissenschaften No. 110, p. 69.

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van't Hoff showed that the following relation exists:

$$K = \frac{0.01991T^2}{W}$$

Herein  $K$  is the molecular depression of the given solvent,  $T$  the absolute freezing temperature of the same, and  $W$  its latent heat of fusion, that is, the number of calories required to convert one gram of the frozen solvent at the temperature of the freezing-point into the liquid of the same temperature.

By means of this equation the molecular depression of the freezing-point of any solvent can therefore be calculated, if the freezing-point and the heat of fusion are known.

If, for example, we wish to calculate the molecular depression of water by means of this equation, we put

$$T = 273, \quad W = 80 \text{ calories,}$$

$$K = \frac{0.01991 \times 273^2}{80} = 18.5,$$

while experiment has given 18.6 for the value of  $K$ .

The following table gives a summary of the molecular depressions of the freezing-point of various solvents calculated in this way, and the values that experiment (by using equation (1) on p. 175) has yielded.

Name of solvent.	Freezing-point.	Latent heat of fusion in calories.	$K = \frac{0.01991T^2}{W}$	$K = \frac{M\Delta}{p}$
Water.....	0°	80	18.5	18.6
Acetic acid .....	16.7	43.2	38.8	39
Benzene.....	5.4	30	51	49
Benzophenon ...	48	21.5	96	95
Diphenylamin...	54	24	88.8	88

It is further to be noted that by means of the equation

$$K = \frac{0.01991T^2}{W},$$

from the known molecular depression ( $K$ ) of a solvent and its known melting-point ( $T$ ), the unknown latent heat of fusion ( $W$ ) can be calculated.



From the standpoint of the biologist, the great importance of freezing-point determinations lies in the fact that they enable him to ascertain the number of molecules dissolved in a given volume of any body fluid.

We shall later become acquainted with individual examples of this nature, when we have considered the so-called electrolytic dissociation of dissolved substances.

Since frequently, in dealing with the determination of the freezing-point of fluids of physiological importance, only very small amounts of the given liquid are at hand, we shall describe an apparatus which in such cases (for example, in the examination of blood) has certain advantages over those already described. The so-called *depressimeter* of J. F. Eijkman\* is illustrated in Fig. 32. It

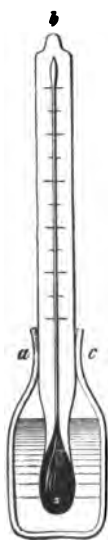


FIG. 32

consists of a flask of about 10 c.c. capacity that has a small thermometer, graduated into tenths or hundredths of a degree, ground into its neck. In dealing with aqueous solutions, the instrument is used in the same way as was described above for the Beckmann apparatus. The separate air-jacket is, however, absent.

If we wish to calculate the osmotic pressure of a solution from the observed depression of the freezing-point ( $\Delta$ ) of the same, the following considerations will yield the result sought. From our equation (1) upon page 175,

$$\Delta = \frac{Kp}{M}$$

The depression of the freezing-point of a cane-sugar solution containing 1 g. of sugar in 100 g. of water is therefore

$$\Delta = \frac{18.6 \times 1}{342} = 0.054^\circ$$

\* Zeitschr. f. physik. Chem. 2, 964 (1888).

We know, upon the other hand, that at  $0^\circ$  the osmotic pressure of this solution amounts to 0.651 atmosphere (see p. 144), wherefore at its freezing-point ( $-0.054^\circ$ ) it is  $0.651(1 - 0.054\alpha) = 0.650$  atmosphere. A depression of the freezing-point of one thousandth of a degree consequently corresponds to an osmotic pressure of  $\frac{0.650}{54} = 0.0120$  atmosphere.\*

We shall now consider how

*b. The Elevation of the Boiling-point*

which dissolved, non-volatile substances impart to a solvent may be used to determine the molecular weight of such substances (*ebullioscopy*).

When water boils, the temperature of the liquid is, as is known to you,  $100^\circ$ , if the barometer stands at 760 mm. If a non-volatile solid, soluble in water, is added to the boiling water, the boiling-point (when the barometer stands at the same height) rises.

For determining this increase the apparatus devised by Beckmann † and illustrated in Fig. 33 is much used. This apparatus consists of an ebullition-tube *A*, with two side tubulations  $t_1$  and  $t_2$ ; through  $t_1$  the weighed substance is introduced into *A*, while  $t_2$  serves for the introduction of a condenser *K*. The ebullition-tube passes through a properly fitted aperture in the asbestos board *L*, and rests upon the wire gauze *K* lying below it. Beneath the stopper *r* the boiling-tube is held in place by the clamp *N*. The wire gauze and the asbestos paper rest upon a ring. As an air-mantel to protect against external cooling, the glass cylinder *G* is used which can be cut from a lamp-chimney,

\* See foot-note on p. 139.

† *Zeitschr. f. physik. Chem.* 4, 532 (1889); 21, 239 (1896). See also the publication of H. Biltz given in the second foot-note on p. 168.

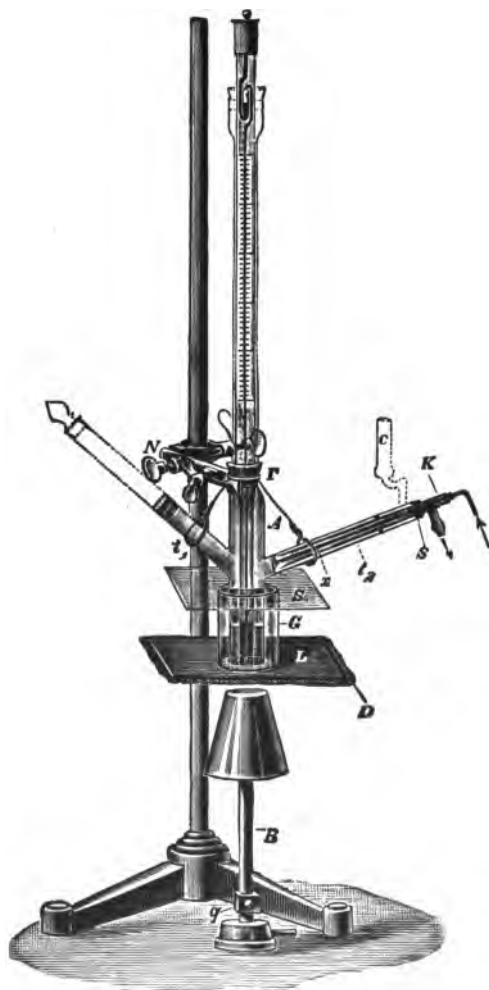


FIG. 33

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and which is closed above by a thin mica plate, or a plate of some other material (glass, asbestos paper).

The dotted prolongation of the vessel *A* and the side tube *t*<sub>1</sub> show how the apparatus may be modified for experiments upon substances that attack the corks.

Upon the side tube *t*<sub>2</sub> is indicated in dotted outline a calcium chloride tube arranged for all cases in which hygroscopic substances are examined, or where the temperature of the water in the condenser lies below the dew-point of the air.

In other cases this may be left off, as also the tight connections between the outer water-tube of the condenser and the tube *t*<sub>2</sub>. In the latter case a thin platinum wire suffices to maintain the position of the condenser at any desired point. The external water-tube *K* is supported upon glass supports to prevent it from touching the tube, and so retaining large layers of liquid. In order to prevent the sudden dripping of condensed liquid back into the boiling-tube, which might be followed by considerable variations in the temperature, the condensing-tube has a fish-tail extremity at its lower end, and does not extend entirely into the ebullition-tube. A horizontally perforated cork cube *g*, pushed over the tube of the burner *B*, serves to regulate the entrance of air in a convenient way.

To produce a regular ebullition of the liquid in the boiling-tube, *A*, a number of small tetrahedrons of platinum-foil are introduced into it. In boiling, the liquid is to cover the bulb of the thermometer completely.

Here, also, it is convenient to introduce the substance to be examined into the ebullition-tube, in the form of a

pastille,\* after the boiling-point of the pure solvent has been determined.

For determining the rise in the boiling-point of *aqueous* solutions, the apparatus of McCoy † and Smits, ‡ which is modelled after that of Landsberger, § is to be particularly recommended because of its simplicity (Fig. 34). *A* is the ebullition-tube (180 mm. long and 30 mm. in diameter) which carries at its upper end a side tube *b*, at its lower end an upturned capillary *a* (3 mm. lumen).

By means of a cork this ebullition-tube is fixed air-tight into a glass flask *B* having a long, wide neck (about 50 mm. lumen). *C* is a lateral tubulation that can be closed with a cork. After *B* is partially filled with water, about 25 c.c. of water are introduced into *A*, which is hung into *B*. A Beckmann thermometer is dipped into the liquid in *A*.

The bulb of the thermometer is surrounded by a cylindrical basket of platinum gauze (height 5 cm., diameter a little less than that of the ebullition-tube). The whole apparatus is set upon copper gauze and heated by an Argand burner. *C* remains open until the water begins to boil; if *C* is closed, the steam from *B* escapes through the tube *a* and leaves the apparatus at *b* after passing through the water in *A*. After some time the water in *A* also begins to boil, and one or two minutes later the thermometer registers a constant temperature.

\* For greater details in the use of the apparatus, see the original paper of Beckmann.

† American Chemical Journal 23, 353 (1900).

‡ Verslagen Kon. Akad. van Wetenschappen te Amsterdam, June 1900.

§ See Landsberger, Ber. d. d. chem. Gesellsch. 31, 358 (1898); Zeitschr. f. anorg. Chem. 17, 422 (1898). Walker and Lumsden, Jour. of the Chem. Soc. 73, 502 (1898).

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After this has been read off, the tube *C* is opened, the thermometer is removed from the ebullition-vessel, and a weighed amount of substance is introduced into the vessel. The thermometer is set back into place, *B* is

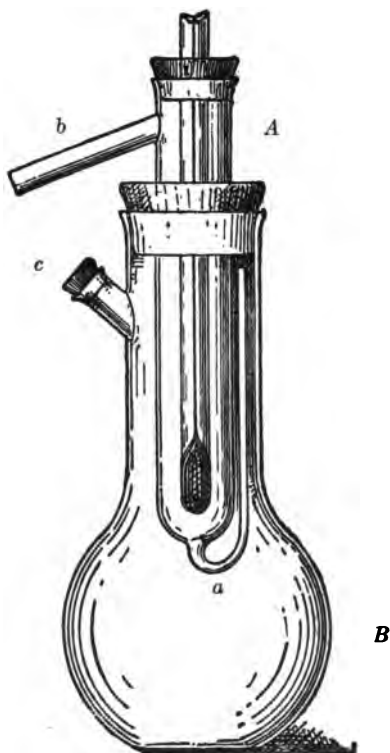


FIG. 34.

heated, and after ebullition has commenced the opening *C* is closed.

About one and a half minutes after the solution in *A* has reached its boiling-point (the boiling-point remains con-

stant to  $0.001^{\circ}$  for about three minutes), the tube *C* is quickly opened, *b* is closed with a cork, *A* is taken out of *B*, and the apparatus is permitted to cool. *A* (with the thermometer) is then placed upon a scale sensitive to centigrams.

If now the ebullition-vessel with the thermometer has been weighed before the experiment, all the data for determining the concentration of the solution are known. We know, therefore, the increase in the boiling-point of a solution the concentration of which is known.

It is to be noted that in all determinations of the boiling-point the height of the barometer is an important factor. In aqueous solutions an increase of 1 mm. in the height of the barometer corresponds to a rise in the boiling-point of about thirty-six thousandths of a degree. For

at 760.00 mm. pressure the boiling-point of water equals  $100.0^{\circ}$ ,  
 " 762 727 " " " " " " " " " 100.1 $^{\circ}$ .

An increase in the height of the barometer of 2.727 mm. therefore corresponds to a rise in the boiling-point of the water of  $0.1^{\circ}$ , wherefore a rise of 1 mm. corresponds to a rise in the boiling-point of  $0.036^{\circ}$ .

If, therefore, the boiling-point of pure water and that of a solution have been observed at different heights of the barometer, a correction corresponding to the same is to be made. The experiment can, however, be conducted in such a way that one is independent of accidental variations in the thermometer during the progress of the experiment.

Two boiling-point apparatus are then employed. Into the first is put pure water, while by means of the second the boiling-point of the pure water is first determined, and

then that of the solution. A change in the height of the barometer during the experiment will then be evidenced by a change in the boiling-point of the water in the first apparatus, and can be taken into account.

If now we investigate, in the manner described, the rise in the boiling-point that solvents show upon the addition of any non-volatile substance, it is found that in dilute solutions the rise in the boiling-point is proportional to the concentration of the dissolved substance.\*

The following table gives the necessary evidence for the same. The table refers to aqueous solutions of cane-sugar. Under  $m$  is given the number of mols of sugar per 100 g. of water;  $t$  is the observed rise in the boiling-point. Further, the value  $\frac{t}{m}$  has been calculated, that is, therefore, the (theoretical) rise in the boiling-point that a solution would show in case it contained one mol of the dissolved substance per 100 g. of water. This last figure ( $K_1$ ) is called the *molecular elevation* of the boiling-point of the water.

$m$	$t$	$K_1$
0.0333	0.17	5.099
0.0999	0.51	5.099
0.1332	0.69	5.174

If, in a similar manner, the rise in the boiling-point brought about by other substances (such as urea, etc.) when one mol of the same is dissolved in each 100 g. of water, is determined, the same value is found for  $K_1$ .

As the mean of many determinations that have been made upon the aqueous solutions of widely differing substances,  $K_1$  has been found to be equal to 5.2.

\* See the analogous behaviour of the freezing-point on p. 174.



This figure therefore means that when one mol of any substance \* is dissolved in 100 g. of water the rise in the boiling-point amounts to 5.2°. (This solution would therefore boil at 105.2° when the barometer stands at its normal height.) Every solvent has a value of its own for the molecular elevation of the boiling-point ( $K_1$ ). In the following table these values are given for a few solvents:

	Water.	Acetic acid.	Benzene.	Ethyl alcohol.	Ether
Molecular elevation of the boiling-point ( $K_1$ ).....	5.2	25.3	26.7	11.5	21.2
Boiling-point (at 760 mm.).	100	118	80	78	35

If the molecular weight of the dissolved substance is unknown, but the molecular elevation of the boiling-point of the solvent is known, then by determining the elevation of the boiling-point of a solution containing a known amount of dissolved substance the unknown molecular weight of the substance can be found.

If we represent by  $\delta$  the experimentally determined elevation of the boiling-point which 100 g. of a solvent show upon the addition of  $p$  grams of substance, and by  $K_1$  the molecular elevation of this solvent, then, when  $M$  is the unknown molecular weight of the given substance,  $\frac{M}{p}$  mols of substance are present in 100 g. of the solvent.

Now since one mol of dissolved substance in 100 g. of solvent would bring about an elevation of the boiling-point of  $K_1$  degrees, we find the value of  $M$  from the proportion

$$\delta : K_1 = \frac{p}{M} : 1.$$

$$M = \frac{K_1 p}{\delta}. \quad (1)$$

As an example is given the following: The elevation of the boiling-point of a solution of 4.80 g. of salicylic acid,  $C_6H_4(OH)COOH$ ,

\* See foot-note p. 175.

MOLECULAR WEIGHT OF DISSOLVED SUBSTANCES. 187

in 100 g. of ethyl alcohol was found to be 0.405°. Since  $K_1$  for ethyl alcohol (see the table upon p. 186) is equal to 11.5,  $M$  is calculated from the equation

$$M = \frac{11.5 \times 4.80}{0.405} = 136,$$

while the formula  $C_4H_4(OH)COOH$  gives the figure 138.

If the molecular weight ( $M$ ) of a dissolved substance is known, and the elevation of the boiling-point ( $\delta$ ) of a solution containing  $p$  grams of dissolved substance in 100 g. of solvent has been determined, then the molecular elevation of the boiling-point ( $K_1$ ) can be calculated from equation (1):

$$K_1 = \frac{M\delta}{p}.$$

Just like the molecular depression of the freezing-point, the molecular elevation of the boiling-point can be deduced from thermodynamical considerations (van't Hoff-Arrhenius \*). If the boiling-point of a solvent according to the absolute temperature scale is  $T_1$ , its latent heat of vaporisation (that is, the number of calories required to convert one gram of the solvent at the boiling-point into vapour of the same temperature)  $W_1$ , then according to Arrhenius

$$K_1 = \frac{0.01991 T_1^2}{W_1}.$$

If, for example, we wish to find the molecular elevation of the boiling-point of water according to this formula, then  $T_1 = 100 + 273 = 373$ ;  $W_1 = 536.6$  calories.

$$K_1 = \frac{0.01991 \times 373^2}{536.6} = 5.16.$$

In a way entirely analogous to that which has before been described in the discussion of the molecular depression of the freezing-point, the unknown latent heat of vaporisation ( $W_1$ ) can be cal-

\* Zeitschr. f. physik. Chem. 4, 550 (1889).

culated by the above equation from the known molecular elevation ( $K_1$ ) and the known boiling-point ( $T_1$ ) of a solvent.

If, further, from the observed elevation of the boiling-point ( $\delta$ ) of a solution we wish to calculate its osmotic pressure, we have but to remember that the elevation of the boiling-point of a 1 per cent solution of sugar is calculated according to equation (1) on page 186 as

$$\delta = \frac{K_1 p}{M},$$

wherein  $K_1 = 5.2$ ,  $p = 1$ ,  $M = 342$ ;

wherefore  $\delta = \frac{5.2 \times 1}{342} = 0.015^\circ$ .

But the osmotic pressure of this solution at  $0^\circ$  equals 0.651 atm., wherefore at the boiling-point,  $(100 + 0.015^\circ) = 100.015$ , it equals  $0.651(1 + \alpha t) = 0.651 \left(1 + \frac{100.015}{273}\right)$  atm. = 0.8892 atm.

An elevation of the boiling-point of fifteen-thousandths of a degree accordingly corresponds to an osmotic pressure of 0.8892 atm., and one of one-thousandth of a degree to an osmotic pressure of  $\frac{0.8892}{15} = 0.0592$  atm.\*

\* See foot-note on p. 139.

## ELEVENTH LECTURE.

### The Theory of Electrolytic Dissociation.

JUST as the gas laws of Boyle and Gay-Lussac may be summed up in the words: the product of the pressure and the volume of a certain weight of gas is proportional to the absolute temperature, so the laws of Boyle-van't Hoff and Gay-Lussac-van't Hoff, which we have found tenable for dilute solutions, may be stated in a similar form: the product of the osmotic pressure and the volume of a certain amount of dissolved substance is proportional to the absolute temperature.

If the osmotic pressure is represented by  $P$ , the volume of the solution by  $V$ , the absolute temperature by  $T$ , then the above law may be stated thus:

$$PV = RT, \quad (1)$$

in which  $R$  is a numerical factor that we call the gas constant, and which for undissociated gases and for many solutions has the same value, 1.991.

While certain substances, like cane-sugar, urea, etc., when dissolved in water obey the above laws, and in consequence exert an osmotic pressure that can be calculated from the above equation, it was found, soon after the enunciation of these laws, that such important groups of substances as the strong inorganic acids, bases, and salts showed marked digressions from the general laws.

The osmotic pressure of these substances, as also the depression of the freezing-point (cf. p. 179) and the elevation of the boiling-point (cf. p. 188) corresponding to this pressure, were found to be greater than one would expect from the above equation.

In order to bring the osmotic pressures as determined by experiment into harmony with the above equation, van't Hoff introduced a factor which he called  $i$ , and wrote the equation (1) for such substances as showed variations from the laws of van't Hoff as follows:

$$PV = iRT. \quad (2)$$

In this equation  $i$  therefore represents how many times greater, as determined by experiment, the osmotic pressure of a certain solution is than one would calculate from the equation

$$PV = RT.$$

Arrhenius found, for example, that a solution which contained 0.682 g. NaCl per 100 g. of water showed a depression of the freezing-point of  $0.424^\circ$ ; 1 mol or 58.5 g. NaCl in 100 g. of water would, according to this, have given a depression of the freezing-point of

$$\frac{58.5}{0.682} \times 0.424 = 36.3^\circ.$$

But we have seen above that the molecular depression of the freezing-point of water is equal to  $18.6^\circ$ . The depression of the freezing-point (and similarly the osmotic pressure  $P$ , which is proportional to it) is therefore in this solution  $\frac{36.3}{18.6} = 1.95$  times greater than the law  $PV = RT$

would indicate. According to this,  $i$  in this case is 1.95, and the behaviour of the solution can be expressed thus:

$$PV = 1.95RT.$$

At the time of the discovery of the laws of osmotic pressure, similar deviations from the gas laws of Boyle-Gay-Lussac were known. In those cases in which these exceptions existed, that is to say, in those cases in which experiment gave a greater value to the pressure exerted by a certain amount of gas than could be calculated from the equation  $PV = RT$ , it was found that the particular gas concerned underwent dissociation, in other words, broke up, either partially or entirely, into part molecules.

If, for example, ammonium chloride ( $\text{NH}_4\text{Cl}$ ) is heated, it is converted into a gas; a part of the  $\text{NH}_4\text{Cl}$  molecules are converted into  $\text{NH}_3$  and  $\text{HCl}$ . The result of this dissociation is that the pressure of the gas increases more rapidly than one would expect from the increase in temperature, since there are now in a given volume of the gas, instead of one molecule ( $\text{NH}_4\text{Cl}$ ), two molecules ( $\text{NH}_3 + \text{HCl}$ ).

Now since with gases such an abnormal rise in gas pressure is explained by a dissociation of the molecules, van't Hoff believed it possible that his laws of osmotic pressure might also stand, since Arrhenius had by letter pointed out to him the possibility that in acids, bases, and salts, which seemed exceptions to the laws of osmotic pressure when dissolved in water, he was perhaps dealing with a dissociation of the molecules into ions.\*

\* Zeitschr. f. Physik. Chem. 1, 481 (1887).

Before we enter upon this subject more fully we shall discuss our conceptions of *electrolytes*, *electrolysis*, and *ions*.

An *electrolyte* (this name, as well as the further nomenclature upon this subject, dates from the observations of Faraday,\* 1791-1867) is a chemical compound which when molten or in solution conducts an electric current. When such a current passes through the electrolyte, or through its solution, the latter undergoes certain changes that are grouped under the name *electrolysis*.

The places at which the electric current enters or leaves the electrolyte (or its solution) are called the *electrodes*. Metals or carbon are mostly used as electrodes.

We distinguish between the two electrodes by the terms *anode* and *cathode*. The electrically charged particles, the aggregation of which constitutes a molecule of the electrolyte are called the *ions* of the electrolyte. The ions which under the influence of the electric current migrate to the anode are called the *anions*, those which wander to the cathode the *cathions*, of the electrolyte.

Thus, for example, NaCl is an electrolyte; Na<sup>+</sup> and Cl<sup>-</sup> are its ions.† Na<sup>+</sup> is the cation, Cl<sup>-</sup> the anion; in the electrolysis of a NaCl solution the cation (Na<sup>+</sup>) wanders to the cathode, the anion (Cl<sup>-</sup>) to the anode.

According to Clausius‡ the constituents (ions) of a greater or less number of the dissolved molecules exist in a free state, and move in all directions through the solution even before the passage of an electric current. Only the

\* Experimental Researches, Ostwalds Klassiker der exakten Wissenschaften No. 81, 86, 87. Leipzig 1896-97.

† As Ostwald has suggested, the cathions and anions of a substance can be indicated by <sup>+</sup> and <sup>-</sup>.

‡ Poggendorffs Annalen 101, 338 (1857).

presence of free ions makes it possible that such a solution can at all conduct electricity, for, according to Faraday's observations, a migration of electrical charges, such as occurs in the conduction of electricity by electrolytes, is possible only through a migration of the ions that carry such charges.

If we dissolve crystals of sodium chloride in water, then, according to Clausius' hypothesis, a part of the NaCl molecules split into the ions Na<sup>+</sup> and Cl<sup>-</sup>; if an electric current is passed through such a solution, the ions, which at first were moving in all directions, are oriented, and the free positive ions, under the influence of the current, are driven in one direction, while the free negative ions are driven in the other.

When the ions reach the electrodes, they can there part with their electrical charges—discharge themselves. According to this idea, it is not the action of the electric current but the act of solution that gives rise to the free ions.

So, for example, pure 100 per cent sulphuric acid does not conduct the electric current. There are therefore no free ions present in it. If we add water to the acid, the water dissociates the sulphuric acid, in other words, free ions are formed. The presence of these makes the mixture a ready conductor of electricity.

The ability of the water (or any other solvent) to split a substance into its ions is called the "dissociating power" of the water. This power varies greatly with various solvents; water has of all the substances thus far examined the greatest dissociating power,\* yet formic acid,

\* Perhaps the dissociating power of hydrogen peroxide is greater than that of water. Compare Calvert, *Drudes Annalen* 1, 483 (1900).



methyl alcohol, ethyl alcohol, acetone, sulphurous acid, and ammonia also have this power. To which properties of these substances is to be attributed their dissociating power is not yet clearly established.\*

That free ions are actually present in the aqueous solution of an electrolyte, and that these are not first produced therein by the action of the electric current, is proven by the following experiment of Ostwald (Fig. 35).

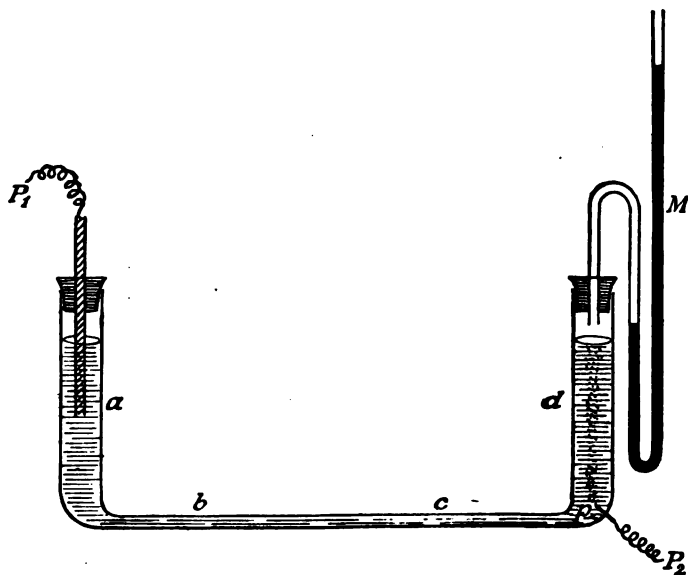


FIG. 35.

Into the U-shaped glass tube *abcd* is poured some dilute sulphuric acid; *bc* is narrow and about 40 cm. long, while *a* and *d* each have the diameter of a test-tube. *a* and *d* are

\* Cf. the literature collected upon this subject by H. C. Jones, *Am. Chem. Jour.* 25, 232 (1901).

closed with caoutchouc stoppers. An amalgamated zinc bar to which has been soldered a copper wire  $P_1$  is passed through the cork into  $a$ . A manometer filled with water and slightly coloured by the addition of a trace of methylene blue passes through the cork in  $d$ . At  $p$  a platinum wire  $P_2$  is fused into the glass.

If  $P_1$  is connected with the positive pole of a storage battery consisting of some five or six cells, an *immediate* evolution of hydrogen is noted at the platinum wire  $p$ , when  $P_2$  is connected with the negative pole.

If, in order to produce the hydrogen, the current had first to dissociate the sulphuric acid, then both of the hydrogen ions which the zinc liberates from the  $\text{SO}_4$ -ion would have to travel the distance  $abcp$  (more than 40 cm.) before they could be given off as free hydrogen at  $p$ . But experiments \* in this direction and mathematical calculations have shown that several hours are required for the migration of the ions through such a distance. Now since it has been found that hydrogen is produced the instant the circuit is closed, we may conclude that free hydrogen ions are present in the vicinity of  $p$  before the closure of the circuit; when the current is closed, these ions give up their electrical charges to  $p$  and show themselves in their neutral electric state—as a gas—in the solution.

Arrhenius,† using for his starting-point the hypothesis of Clausius and the facts that had been learned from the

\* Nernst, *Zeitschr. f. Electrochemie* 3, 308 (1896-1897). O. Lodge, Report of the British Association, 1887, 589. W. C. Dampier Whetham, *Philosophical Transactions of the Royal Society* 184, 337 (1894). Masson, *Zeitschr. f. physikal. Chemie* 29, 501 (1899).

† *Zeitschr. f. physik. Chem.* 1, 631 (1887).

dissociation of dilute gases, formulated a theory which explains both qualitatively and quantitatively the exceptions which certain substances in dilute solution show to the simple laws of van't Hoff. We shall now study this theory, *the theory of electrolytic dissociation* (we apply the term electrolytic dissociation to the splitting of the electrolyte into its ions) more closely.

We have seen that the deviations which under certain conditions dilute gases show to the laws of gas pressure can be explained by the dissociation of the substances under consideration into smaller molecules. In the same way Arrhenius attributes the exceptions shown by certain substances when in dilute solution to the laws of osmotic pressure to the dissociation of these substances into their constituent ions.

If, for instance, we dissolve NaCl in water, the NaCl dissociates in part into the ions Na<sup>+</sup> and Cl<sup>-</sup>.<sup>\*</sup> Each of these ions conducts itself like a molecule and exerts its individual osmotic pressure. The osmotic pressure of a substance in solution (which can be determined either by Pfeffer's osmometer, the depression of the freezing-point, or the elevation of the boiling-point) is therefore equal to the sum of that of the undissociated molecules and the ions that result from the dissociated molecules.

Now if by any means it could be determined what proportion of the dissolved molecules had undergone dissociation into ions, it would be possible to calculate the osmotic

<sup>\*</sup> That free ions, such as sodium ions, can exist in the water without giving rise to the formation of NaOH and H, as is the case with the metallic sodium, is to be attributed to the electrical charge of the Na ion. It is the electrical charge of the Na ion that distinguishes it from the electrically neutral (metallic) sodium.

pressure of the solution of an electrolyte by van't Hoff's law. This is intelligible when we remember that if the number of (undissociated) molecules and ions in a certain volume are known, we know the sum total of molecules that contribute to the osmotic pressure, for each ion conducts itself as an individual molecule.

It becomes evident, at the same time, that the osmotic pressure of a solution in which the dissolved substance is split into ions must be greater than that of a solution into which the same number of molecules of the substance are introduced, but where no electrolytic dissociation occurs; for since the ions conduct themselves as independent molecules, there are present in a definite volume of the first solution a greater number of molecules than in an equal volume of the second, and the greater the number of molecules present in the given volume, the greater is the osmotic pressure of the solution.

If we wish to deal with the quantitative side of this question, we have to discover a means of ascertaining what part of an electrolyte is broken up into ions when it goes into solution; in other words, a means of determining the *degree of dissociation* of the electrolyte. Arrhenius has pointed out the way by which this may be accomplished. If an electrolyte is dissolved in water, a part of its molecules are dissociated into their constituent ions. The molecules that undergo dissociation are known, after Arrhenius, as the *active* molecules, in contrast to those which do not undergo dissociation, the *inactive* molecules.

If the number of active molecules in a certain volume of solution is represented by  $n$ , the number of inactive molecules by  $m$ , there are in all, if each active molecule dissociates in  $k$  ions,  $m+nk$  particles in the solution.

So far as the value of  $k$  is concerned, it need only be pointed out that for NaCl it is 2, since each molecule of NaCl dissociates into two ions (Na' and Cl'); that for BaCl<sub>2</sub> the value \* of  $k=3$  (Ba·· and Cl', Cl').

Arrhenius assumes that at great dilution all the inactive molecules are rendered active,—in other words, in very dilute solution all the molecules of a dissolved substance are broken up into ions.

By the degree of dissociation ( $\alpha$ ) of a dissolved electrolyte we understand the relation that exists between the number of the active and the sum of the active and inactive molecules. According to definition, therefore,

$$\alpha = \frac{n}{m+n}.$$

We shall now prove that a simple relation exists between the value  $\alpha$  and the value  $i$ , which, as we have seen, shows how many times the osmotic pressure of a solution, as found by experiment, is greater than that calculated from the equation  $PV=RT$ .

We notice, first of all, that the osmotic pressure of solutions of electrolytes as determined by the latter equation is too low, because we have considered in our calculations only the number of molecules that are dissolved in the solution. But, as we now know, some of these molecules suffer a dissociation into their constituent ions, each of which conducts itself as an independent molecule. In the act of solution the number of molecules has therefore been increased.

\* Electrolytes which, like NaCl, dissociate into two ions are called *binary*; those which, like BaCl<sub>2</sub>, dissociate into three ions are known as *ternary* electrolytes.

According to this,  $i$  represents the relation between the number of molecules that are actually present in the solution and the number that would be present if dissociation had not taken place.

How many molecules, then, are there really in the solution? First,  $m$  inactive, then  $n$  active, each of which furnishes  $k$  ions (molecules), making a total of  $m+nk$  molecules.

The number of molecules present, if no dissociation occurred, would evidently be  $m$  inactive +  $n$  active molecules, making a total of  $m+n$  molecules.

From this it follows that

$$i = \frac{m+nk}{m+n}.$$

But

$$\alpha = \frac{n}{m+n}.$$

From these two equations we get

$$i = 1 + (k-1)\alpha.$$

If now a method were at hand by which the degree of dissociation of an electrolyte in solution could be determined, then  $i$  could be calculated, and this value should correspond, if our previous considerations have been correct, with the value of  $i$ , as obtained by determining the depression of the freezing- or the elevation of the boiling-point of the solution under consideration. We may express these conclusions in another way: by determining the value of  $\alpha$  we can arrive at the value of  $i$ , by which  $RT$  in the equation of van't Hoff,  $PV = RT$ , must be multiplied in order that it may hold for the solution of the electrolyte under consideration.

We can determine the degree of dissociation  $\alpha$  of an electrolyte in solution, according to Arrhenius, from its electrical conductivity.

#### THE DETERMINATION OF ELECTRICAL CONDUCTIVITY.

(METHOD OF KOHLRAUSCH.)

Before we enter more fully into a discussion of the determination of  $\alpha$ , I wish to bring to your notice the beautiful observations of F. Kohlrausch, an understanding of which

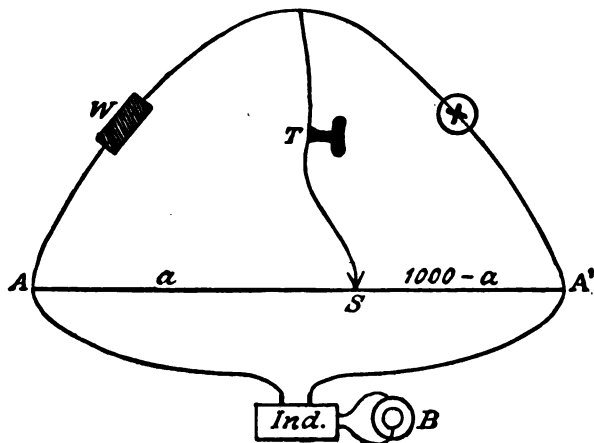


FIG. 36.

is essential in order to comprehend the facts to be considered later.\* These observations were begun years before the development of the theory of electrolytic dissociation, and have been continued to the present time.

\* The observations in this direction are found in Kohlrausch and Holborn, *Das Leitvermögen der Elektrolyte*, Leipzig 1898. The method here described is especially adapted to the uses of the physiologist and biologist.

Kohlrausch determined the resistance that solutions of various electrolytes at various concentrations offer to the passage of the electric current. The method which he evolved for this purpose, and which yields most accurate results, is as follows:

The resistance of the solution under investigation is measured by the Wheatstone bridge, by comparing the resistance of the solution (at a definite temperature) with a known resistance in the Wheatstone bridge. In Fig. 36 is given a sketch of the apparatus, which we shall now describe.  $X$  is a vessel containing the solution the resistance of which is to be determined (resistance-cell). Resistance-cells may be of various kinds, depending upon the amount of resistance that the solution under investigation offers to the electric current. Fig. 37 shows the form suggested by Arrhenius, which is widely used.

Two strong circular platinum discs, 3 to 4 cm. in diameter, are welded to stout platinum wires and soldered with gold. These wires are fused into the glass tubes  $b_1$  and  $b_2$ , which are fastened into the ebonite cover  $d$  of the vessel  $aa$  by means of fish-glue or some other similar substance.

The cover is deeply grooved so as to fit securely over the lip of the container. A thermometer  $t$  passes into the solution through a hole in the cover.  $b_1$  and  $b_2$  are filled with mercury into which pass the thick copper wires  $g_1$  and  $g_2$ , which can be connected with the Wheatstone bridge.

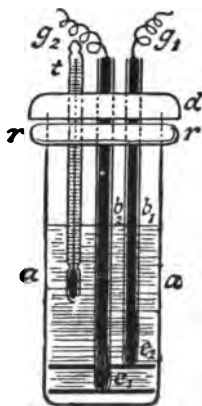


FIG. 37.



The distance between the electrodes  $e_1$  and  $e_2$  is increased or diminished according as we deal with solutions of low or high resistance.

The vessel  $aa$  must always be filled to the same height; it is therefore well to scratch a mark upon the wall of the glass tube with a diamond. A thick rubber ring is passed over the upper end of the glass cylinder  $aa$ ; the apparatus is slipped into a hole in a board and supported upon the edge of the thermostat pictured in Fig. 1, so that  $aa$  is immersed in the water. The rubber ring prevents the apparatus from slipping through the opening in the board into the thermostat.

The platinum electrodes  $e_1$  and  $e_2$  are *platinised*, that is, covered with a coat of platinum-black (finely divided platinum). By this means the so-called *tone minimum* of the telephone, of which we shall speak immediately, is in most cases rendered more distinct.

The electrodes are platinised in the following way: A solution having the composition given below\* is introduced into the resistance-cell (Lummer and Kurlbaum).

30 g. water,  
1 g. chloride of platinum,  
0.08 g. acetate of lead.

The wire  $g_1$  is then connected for two to three minutes with the positive pole of a storage battery, while  $g_2$  is connected with the negative pole, after which the current is reversed. A fairly vigorous evolution of gas results. After about ten minutes both of the originally bright platinum electrodes, previously washed in concentrated nitric acid, are covered with a black velvety layer of finely divided platinum. The electrodes are placed for several

\* Kohlrausch and Holborn, l. c. p. 9.

days in water which is frequently renewed, in order to remove the platinising solution, which clings quite tenaciously to the coverings of the electrodes.

A convenient apparatus, and one that is to be recommended because the electrodes are protected against displacement, is the so-called immersion electrode of Kohlrausch (Fig. 38). Two strips of platinum-foil,  $e_1$  and  $e_2$ , are wound about the glass tube  $aabb$  and fastened there by means of thin platinum wires. These strips of platinum constitute the electrodes. A glass hood  $sv$ , drawn out at  $vv$  and fused to the tube  $aabb$ , protects the electrodes against displacement. The lower end of the hood is open, while a small aperture  $o$  at its upper end permits the air to escape when the apparatus is dipped into a solution.

The constriction  $vv$  serves to increase the resistance between the electrodes. Two capillary tubes are fused into the glass tube  $aabb$  by means of the glass supports  $s s s$ . Into the lower ends of these tubes are fused the fine platinum wires,  $d_1$  and  $d_2$ , which are connected with the electrodes.  $k_1$  and  $k_2$  are filled with mercury, and are connected with the Wheatstone bridge by means of copper wires.

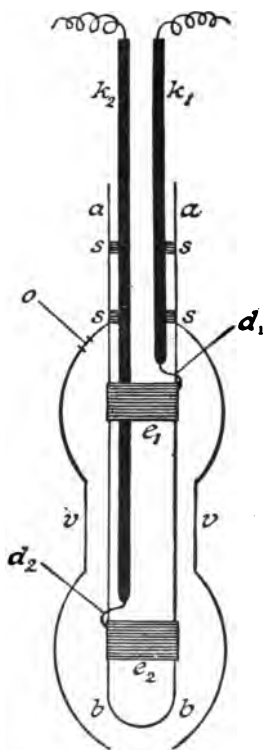


FIG. 38.

The entire immersion electrode is dipped into a small glass cylinder containing the solution of which the resistance is to be determined. Care is taken, however, that the opening  $o$  is never covered by the solution. The electrodes  $e_1$  and  $e_2$  are platinised in a way similar to that described above.

We return now to the diagram shown in Fig. 36.  $W$  is a rheostat (resistance-box) by means of which different lengths of wire having various resistances may be introduced into the circuit.

$AA$  is a thin platinum wire stretched along a one-metre wooden scale divided into millimetres. Upon this wire, which must have the same electrical calibre throughout\*—that is, equal lengths of wire must offer equal resistances to



FIG. 39.

the electric current—moves the sliding contact  $S$ , pressure upon which brings it in contact with the wire.

$T$  in Fig. 36 is a sensitive telephone, while  $Ind.$  represents a very small Ruhmkorff induction-coil connected with the storage battery  $B$ . The induction-coil should give a sound of high pitch. In order that there may be no disturbance from this sound when the apparatus is used, the induction-coil is placed in a felt-lined box.

If the resistance of a solution contained in the vessel  $X$

\* Every wire used for such measurements must be examined in this particular from time to time. A convenient method is that of Strouhal and Barus, *Wied. Ann.* 10, 326 (1880). Kohlrausch and Holborn, l. c. p. 45.

is to be determined, a certain resistance is introduced into the rheostat after the induction-coil has been set in motion, and the sliding contact  $S$  is moved along the wire  $AA$  until the telephone no longer sounds. Since in most cases it is impossible to get the telephone absolutely quiet, two points are sought along  $AA$  where the tone has the same intensity, and the average of these two readings is taken as the minimal point.

When the telephone is quiet, the branch circuit into which it has been introduced has no current flowing through it, and conditions may then be represented by the following:

$$X : W = (1000 - a) : a,$$

wherefore

$$X = W \frac{(1000 - a)}{a}.$$

Since by experiment  $W$  and  $a$  (therefore also  $1000 - a$ ) are known,  $X$  is also known.

If the rheostat (resistance-box)  $W$  is divided, for example, into ohms, we know from the experiment the resistance of the solution, expressed in ohms.\*

But the resistance between the two electrodes which is offered to the electric current by a solution in the resistance-cell is dependent, among other things, upon the distance between the electrodes and their dimensions. The less the distance between the electrodes or the greater their dimensions, the less is the resistance, and *vice versa*. If, now, we wish to compare the measurements made by various observers with various resistance-cells, we shall have to express all these measurements in terms of the same system.

\* Later we shall define this resistance more accurately.

This system of measurements has been established with great accuracy through investigations recently carried out in the *Physikalisch-Technische Reichsanstalt* of Charlottenburg, and it would be well if medical literature, in which great confusion has thus far reigned in this direction, would make use of it. Were this done, the extensive corrections which one is now compelled to make in reading the discourses of various authors would be done away with.

As the unit of conductivity (the conductivity of a substance is equal to the reciprocal of its resistance) we take the conductivity of a cube of any substance which measures one centimetre on each side and has a resistance of 1 ohm. Conductivity as expressed in this unit is designated by  $\kappa$ .

If, therefore, a solution between two electrodes having a surface of 1 sq. cm. and placed 1 cm. apart has a resistance of  $\frac{1}{\kappa}$  ohm, the conductivity of this solution is  $\kappa$ .

The equivalent conductivity ( $\Lambda$ ) of a solution is the conductivity ( $\chi$ ) of this solution divided by the number of gram-equivalents of the dissolved substance present in each c.c. of solution. If the number of gram-equivalents per c.c. equals  $\eta$ , then  $\Lambda = \frac{\kappa}{\eta}$ .

It is to be noted that for univalent electrolytes (as NaCl) the equivalent weight (58.5) and the molecular weight (58.5) are the same, while for bivalent electrolytes (as  $H_2SO_4$ ) the equivalent weight (49) is one-half the molecular weight (98). The molecular conductivity of a bivalent electrolyte is therefore twice its equivalent conductivity.

If we wish to reduce the resistance (or the conductivity) of a solution, as measured by any resistance vessel, to this unit, we have to determine, first of all, the so-called *resistance capacity* of the apparatus employed. If we call this  $C$ , then we understand thereby the resistance which a solution the conductivity of which is unity would have in this vessel.

If a solution having a conductivity of  $\kappa$  has a resistance  $X$  in the resistance vessel, then

$$\begin{aligned} X &= \frac{C}{\kappa}, \\ \text{or} \quad C &= \kappa X. \end{aligned} \tag{1}$$

In order to determine the resistance capacity, the resistance vessel is filled with a solution the conductivity ( $\kappa$ ) of which is known, and the resistance ( $X$ ) of the solution when in the vessel is measured. From this measurement we determine by equation (1) the value of  $C$ .

If  $C$  has been once ascertained, it is known for all time, after which any solution the conductivity of which is to be determined may be put into the vessel and its resistance ( $X_1$ ) found. The conductivity ( $\kappa_1$ ) of such a solution may then be calculated from the equation

$$\kappa_1 = \frac{C}{X_1}.$$

If now the value of  $X_1$  has been determined by the Wheatstone bridge for a solution the equivalent conductivity of which we wish to ascertain by the equation

$$X_1 = W_1 \frac{1000 - a_1}{a_1} \text{ (compare p. 205).}$$

in which  $W_1$  is the resistance in the rheostat  $W$  (Fig. 36) when the telephone is quiet, and  $a_1$  is the wire to the left of the slider, then

$$\kappa_1 = \frac{C}{X_1} = C \frac{a_1}{W_1(1000 - a_1)}.$$

From which follows that the equivalent conductivity of the solution investigated is

$$\Lambda = \frac{\kappa_1}{\eta} = \frac{C}{\eta} \frac{a_1}{W_1(1000 - a_1)}. \quad (2)$$

Since in this equation  $C$ , the resistance capacity of the resistance vessel employed, when once determined, has a constant value for a given vessel, and since  $\eta$  is known if we know the concentration of the solution under investigation, that is to say, if we know the number of gram-equivalents of the dissolved substance present in each c.c. of solvent; and since  $a_1$  and  $W_1$  can be read from the apparatus, we know also the value of  $\Lambda$ , the equivalent conductivity of the solution under consideration.

Since the equivalent conductivity of a solution varies greatly with changes in temperature (an increase of  $1^\circ$  brings about an increase in the equivalent conductivity of about 2 per cent), the resistance vessel containing the solution must be kept in a thermostat.

A practical example may serve to elucidate the foregoing. Suppose the molecular conductivity of a  $\frac{1}{4}$  normal sodium chloride

solution at 25° were to be determined. Since NaCl is a univalent electrolyte, the molecular and equivalent conductivity are the same.

We determine, first of all, the resistance capacity ( $C$ ) of the resistance vessel. For this purpose the vessel is filled with a solution the conductivity of which has been determined by other means. For example, a  $\frac{1}{10}$  normal KCl solution in which  $\kappa$  at 25° equals 0.002765\* is chosen. The resistance vessel is introduced into the circuit of the Wheatstone bridge, and the value of  $a$  on the wire  $AA$  is determined by finding the point where the telephone is silent or the tone minimum is reached, when the resistance  $W$  is in the rheostat. If it is found that when

$$\begin{aligned} W &= 75 \text{ (ohms),} \\ a &= 525 \text{ (scale divisions),} \end{aligned}$$

then the resistance of the  $\frac{1}{10}$  normal KCl solution in our resistance vessel is

$$\begin{aligned} X &= W \frac{1000 - a}{a}, \\ X &= 75 \frac{1000 - 525}{525}, \\ X &= 67.85, \end{aligned}$$

and the resistance capacity of the vessel is (see equation (1), p. 206)

$$C = \chi X = 0.002765 \times 67.85 = 0.1876.$$

After the potassium chloride solution has been removed, the  $\frac{1}{10}$  normal NaCl solution the molecular conductivity of which is to be determined is introduced into the resistance vessel and the vessel rinsed several times with this solution.

The resistance  $X_1$  of this solution is now determined by introducing it into the circuit of the Wheatstone bridge.

It is found that the telephone is silent when

$$\begin{aligned} W_1 &= 128, \\ \text{and } a_1 &= 556. \end{aligned}$$

The molecular conductivity of the  $\frac{1}{10}$  normal NaCl solution is therefore

$$\Lambda = \frac{C}{\eta} \frac{a_1}{W_1(1000 - a_1)}. \quad (\text{Compare p. 207.})$$

\* Compare Kohlrausch and Holborn, l. c., Table, p. 204.

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In this equation we have to substitute for  $C$  the value 0.1876 just found, for  $a_1$  the value 556, for  $W_1$  the figure 128, while for  $\eta$ ,  $\frac{1}{64000}$  (the number of gram-equivalents NaCl in 1 c.c. of the solution), since 1 gram-equivalent has been dissolved in 64 litres = 64000 c.c.

$$\text{Hence} \quad A = \frac{0.1876}{1} \frac{556}{128(1000 - 556)},$$

$$A = 117.4$$

Ostwald\* found the value of  $A$  to be 116.9, Walden 117.9, while our figure falls between these two.

Since the conduction of electricity in electrolytes is, according to Faraday's observations, dependent solely upon a transportation of the electrical charges carried by the ions, the molecular conductivity of a solution, *ceteris paribus*, will be dependent upon the number of free ions present in a definite volume of the solution. In other words, according to Arrhenius, the molecular conductivity  $A_v$  at a certain concentration (1 mol of dissolved substance in  $V$  litres of solvent) will be proportional to the degree of dissociation ( $\alpha$ ) of the electrolyte. We can therefore say

$$A_v = K\alpha,$$

in which  $K$  is a numerical factor.

If we further assume with Arrhenius that at very great (infinite) dilution all the molecules are split into their ions, then in this case  $\alpha = 1$ .

The molecular conductivity ( $A_\infty$ ) of such an (infinitely) dilute solution is therefore

$$A_\infty = K\alpha = K \times 1 = K.$$

From the equations

$$A_v = K\alpha$$

\* Compare Kohlrausch and Holborn, l. c., Table, p. 163.



and

$$\Lambda_{\infty} = K$$

we get

$$\frac{\Lambda_v}{\Lambda_{\infty}} = \alpha,$$

or to state it in words: In order to determine the degree of dissociation ( $\alpha$ ) of a solution containing 1 gram-equivalent of dissolved substance in  $V$  litres, determine the equivalent conductivity ( $\Lambda_v$ ) of this solution, and divide it by the equivalent conductivity ( $\Lambda_{\infty}$ ) of a solution containing the same substance in very great (almost infinite) dilution.

The question now arises, How is it possible to determine the conductivity of a solution at infinite dilution? In answer to this question it must be said that it is in reality impossible to make such a determination, but experiment has shown that many substances at a dilution of 1 gram-equivalent in 1000–2000 litres are dissociated into ions to such an extent that further dilution causes practically no alteration in their equivalent conductivity. If we therefore determine the equivalent conductivity of these substances in solutions containing  $\frac{1}{1000}$  to  $\frac{1}{2000}$  gram-equivalent of dissolved substance per litre, we may regard this as the equivalent conductivity at infinite solution ( $\Lambda_{\infty}$ ).

The following table shows that the equivalent conductivity of a neutral salt, such as NaCl, progressively increases until a certain *limit* is reached, after which greater dilution leaves it practically unaltered. The table holds for a temperature of 18°. Under 1000 $\eta$  is given the number of gram-equivalents NaCl per litre. The degree of dissociation of the sodium chloride has been calculated from the formula  $\alpha = \frac{\Lambda_v}{\Lambda_{\infty}}$ , in which 109.7 has been taken as the value of  $\Lambda_{\infty}$ .

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1000 $\eta$ .	Equivalent Conductivity ( <i>d</i> ).	Degree of Dissociation ( <i>e</i> ).
1.	74.4	0.68
0.5	80.9	0.73
0.1	92.5	0.84
0.01	102.8	0.93
0.002	106.7	0.97
0.001	107.8	0.98
0.0002	109.2	0.99
0.0001	109.7	1.00

It can be seen from the table that the equivalent conductivity of a solution containing 0.0002 mol per litre changes but little if the solution is diluted one half, while at a higher concentration dilution (for example, from 0.002 mol to 0.001 mol per litre) causes a well-marked change in the equivalent conductivity.

Since the degree of dissociation  $\alpha = \frac{n}{m+n}$  represents the relation that exists between the number of active (dissociated) molecules and the total number of molecules present in the solution if no dissociation occurred, the fact that  $\alpha = 0.98$  in a solution that contains 0.001 mol NaCl per litre indicates that of each 100 molecules present, 98 have been dissociated into their ions.

In illustration of what has been said, the following table is given in which are shown the equivalent conductivities of a number of salts, acids, and a base at 25°. Under *V* in the first column \* are given the number of litres in which a

\* It may not be superfluous to point out the relation that exists between *V* and  $\eta$ .  $\eta$  gives the number of gram-equivalents of dissolved substance per c.c.; *V* indicates the number of litres in which 1 gram-equivalent of the substance has been dissolved. If 1 gram-equivalent is dissolved in *V* litres, then  $\frac{1}{1000V}$  gram-equivalent of dissolved substance is present in each c.c. of solution, wherefore  $\eta = \frac{1}{1000V}$ , or  $V = \frac{1}{1000\eta} = \frac{1}{10^3} \eta$ .

gram-equivalent of the substance under consideration has been dissolved; the number 32 in this column when applied to NaCl therefore means that  $1 \times 58.5$  g. NaCl have been dissolved in 32 litres. The figures under the various formulæ represent the equivalent conductivities of the substances at 25°.\*

EQUIVALENT CONDUCTIVITY AT 25°.

V.	NaCl.	TiOH.	HClO <sub>3</sub> .	CH <sub>3</sub> COONa.	CH <sub>3</sub> COOH.
32	114.6	230	387	80.5	9.2
64	117.9	238	391	82.7	12.9
128	120.4	244	399	85.1	18.1
256	122.6	248	402	87.0	25.4
512	124.7	248	402	89.0	34.3
1024	125.9	...	402	90.6	49.0

The neutral salts of the strong inorganic acids, such as NaCl, KCl, etc., have the same equivalent conductivity at the same concentrations. As has just been said, by progressive dilution the equivalent conductivity approaches a limit. This is also true for the neutral salts of organic acids, such as sodium acetate, for example.

The degree of dissociation of these substances is great even in concentrated solutions. As the table shows, the degree of dissociation  $\alpha$  for HClO<sub>3</sub> when 1 gram-equivalent (= 1 mol in this case, since HClO<sub>3</sub> is a univalent electrolyte) is dissolved in 256 litres of water is  $\frac{A_{256}}{A_{\infty}} = \frac{402}{402} = 1$ . In other words, chloric acid is totally dissociated at this dilution.

In contrast hereto, the organic acids, such as acetic acid, are only slightly dissociated even in very dilute solutions. Here the equivalent conductivity does not approach a

\* See Kohlrausch and Holborn, where detailed tables of these values may be found.

limit even in solutions having a very low concentration. In these cases it is therefore impossible to determine experimentally the equivalent conductivity at infinite dilution, for if we determine the equivalent conductivity of such a substance even at exceedingly great dilution, we would fall into serious error. Because of the slight dissociation (small number of ions in the unit volume) the conductivity of such a solution would be so low that it would equal the conductivity of the water used in making up the solutions. The presence of slight impurities, which can be removed only with the greatest difficulty, accounts for the slight conductivity shown by the water used in making up the solutions.

We must therefore find another means of determining  $A_{\infty}$  for these slightly dissociated substances. A description of the method of this determination, and the principle upon which it is based, cannot be given here.

We undertook the determination of the degree of dissociation of an electrolyte in solution primarily to determine the value of  $i$  from the equation

$$i = 1 + (k - 1)\alpha$$

(see page 199). I wish to direct your attention once more to this equation.

If, for example, we find that in a sodium chloride solution (at 18°) containing 0.001 mol NaCl per litre  $\alpha = 0.98$  (compare table p. 211), the value of  $i$  for this solution is found from the equation

$$i = 1 + (k - 1)0.98 = 1.98.$$

The osmotic pressure of this solution, or the depression of the freezing-point or elevation of the boiling-point proportional to it, is therefore 1.98 times as great as the os-

otic pressure of this solution calculated from the equation  $PV=RT$ . If for this is substituted the equation

$$PV=1.98RT,$$

then the osmotic pressure of the solution as calculated by the latter equation agrees with the osmotic pressure of the solution as determined by experiment.

It may therefore be said that the laws of van't Hoff for the osmotic pressure of dilute solutions hold good for electrolytes if the dissociation of the dissolved substance is taken into consideration.

If the value of  $i$  has been ascertained for a certain solution by the determination of the depression of the freezing-point or the elevation of the boiling-point, then the value of  $\alpha$  can be calculated from the equation  $i=1+(k-1)\alpha$ .

$$\alpha = \frac{i-1}{k-1}.$$

The following table, which refers to solutions of sodium chloride, shows that  $\alpha$  as determined by different methods has the same value.\*

Concentration (mols per litre).	$\alpha$ By determining the conductivity.	$\alpha$ By determining the depression of the freezing-point.
0.001	0.98	0.984
0.01	0.93	0.905
0.1	0.84	0.841

A word must be said concerning the solvents employed in making the dilute solutions used in conductivity determinations. These solvents must be very pure; that is to

\* Nevertheless exceptions are found which are attributable *in part*, no doubt, to the fact that the freezing-point is determined at a temperature of about 0°, the boiling-point at about 100°, the conductivity at 25°.

say, they must contain not even traces of electrolytes in solution. This becomes evident when we remember that in dealing with the conductivity of very dilute solutions ( $\frac{1}{100}$ ,  $\frac{1}{1000}$ ,  $\frac{1}{10000}$  normal) the traces of impurities originally present in the solvent play an important rôle, since they may contribute as much to the conductivity of the solution under examination as the substance itself the conductivity of which is to be determined. That great value is therefore to be attached to the extreme care exercised in making such investigations becomes self-evident.

All bottles, flasks, etc., which are to come in contact with the solution or solvent under investigation must be steamed before being used (see p. 16).

If we wish to prepare aqueous solutions, which are the most important from the biologist's standpoint, the water to be used is prepared in the following way: 5 g. of glacial phosphoric acid are added to each 40 litres \* of water, which is then distilled in a tinned vessel. The middle portion only of the distillate is used. Great care is of course taken to prevent the water in the distilling-chamber from bubbling over into the receiver.

To free the distillate of any carbonic acid that it may contain which would contribute in no slight way to the conductivity of the water, and to keep the water from absorbing carbon dioxide from the air, the following apparatus is of the greatest service. (Fig. 40.)

The bottle *A* (which has been steamed, and is used exclusively for storing this water) is closed by the rubber stopper *SS*, which is perforated by four openings. Through these openings pass the glass tubes *hg*, *ml*, *fe*, and *ad*, the form of each of which is shown in the illustration.

\* To combine with traces of ammonia that might be present.

After the distilled water has been poured into *A*, *ef* is connected with a glass tube,  $1\frac{1}{2}$  m. long and 1 cm. in diame-

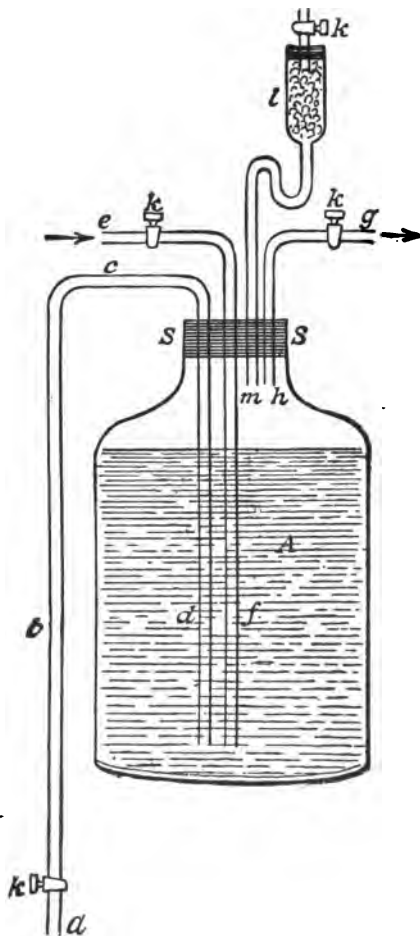


FIG. 40.

ter, filled with powdered sodium hydroxide and a layer of cotton to hold the powder in place, and *g* is connected with

a hydraulic air-pump. A current of air free from carbon dioxide now passes through *ef* into the water and carries out with it any carbon dioxide that may be dissolved in the water. After some six hours the current of air is broken, and the glass stop-cocks *k* and *k* of the tubes *ef* and *gh* are closed. When the water is to be used, it is removed from the bottle by means of the siphon *dcb*; the air entering *A* passes in *l* over powdered sodium hydroxide lying upon a layer of cotton. The bend in the tube prevents the sodium hydroxide dust from falling into the water.

The water even when prepared in this careful manner is still a slight conductor of electricity because of the traces of impurities that are still present therein.

If we dissolve an electrolyte in this water and determine the conductivity of the resulting solution, the observed conductivity therefore equals the sum of the conductivity of the dissolved electrolyte, and the conductivity of the impurities in the water. If the value of the first is to be found, the conductivity of the water (that is to say, of the impurities present in the water) must be subtracted from the total conductivity.

If, for example, we find that for a  $\frac{1}{4}$ N. NaCl solution

$$\kappa_1 = 0.00185,$$

and that for the conductivity of the water used ( $\chi_2$ ) at the same temperature

$$\kappa_2 = 0.00002,$$

then the conductivity of the solution ( $\chi$ ) is

$$\kappa = \kappa_1 - \kappa_2 = 0.00185 - 0.00002 = 0.00183.$$

The equivalent conductivity (see p. 207) of the  $\frac{1}{4}$ N. sodium chloride solution is therefore

$$A = \frac{\kappa}{\eta} = \frac{0.00183}{\frac{1}{64000}} = 117.4.$$



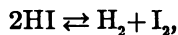
## TWELFTH LECTURE.

### The Theory of Electrolytic Dissociation (Continued).

THE analogy which exists between the behaviour of dilute gases and that of substances in dilute solution has already been pointed out. Not only could this analogy be shown to hold for the non-electrolytes, such as cane-sugar and urea, but also for the electrolytes, provided their electrolytic dissociation is taken into consideration.

Yet in the latter case this analogy may be followed still farther. We have seen before (see p. 75) that when a gas, such as hydriodic acid, dissociates, a definite relation exists between the concentration (the pressure) of the non-dissociated part and that of the products of this dissociation when equilibrium has been established.

I take the liberty of calling to your mind that the condition of equilibrium may here be expressed by the equation



and that when this has been established the following relation exists:

$$K = \frac{p_{\text{HI}}^2}{p_{\text{H}_2} \times p_{\text{I}_2}},$$

in which  $K$  is the equilibrium constant,  $p_{\text{HI}}$  the pressure of the undissociated hydriodic acid,  $p_{\text{H}_2}$  and  $p_{\text{I}_2}$  the partial pressures of the hydrogen and iodine vapour.

This relation we derived from the application of the Guldberg-Waage law to this dissociation.

We shall now inquire in how far the process of dissociation in electrolytes is also governed by this law.

If a binary electrolyte, such as acetic acid, is dissolved in water, it is dissociated in part into its ions,  $\text{CH}_3\text{COO}$  and  $\text{H}$ . Now we know that these ions conduct themselves as independent molecules. If we apply the law of Guldberg and Waage in the same way as we have done in the case of dilute gases, then, in the condition of equilibrium, the following equation must hold:



Herein  $k_1$  is the velocity with which the undissociated molecule breaks up into its ions,  $k_2$  the velocity with which the ions again combine.  $C$  represents the concentration (mols per litre). Now if  $\frac{k_1}{k_2} = K$ , then

$$K = \frac{C_{\text{CH}_3\text{COO}} \times C_{\text{H}}}{C_{\text{CH}_3\text{COOH}}}. \quad (1)$$

Now for each  $\text{CH}_3\text{COO}$  ion in the solution there exists one  $\text{H}$ -ion. Wherefore

$$C_{\text{CH}_3\text{COO}} = C_{\text{H}},$$

and

$$C_{\text{CH}_3\text{COO}} \times C_{\text{H}} = C_{\text{H}}^2.$$

Equation (1) then assumes the following form:

$$K = \frac{C^2}{C_{\text{CH}_3\text{COOH}}}; \quad (2)$$

that is to say, a constant relation ( $K$ ) always exists between the dissociated part and the undissociated part in the solution. The equilibrium constant is here called the *dissociation constant*. It must be remembered that in these considerations it is presupposed that the temperature remains constant.

Now this equation can be stated in another form in which it can more easily be verified by experiment.

If a mol of acetic acid is dissolved in  $V$  litres, and the dissociated part amounts to  $\alpha$ , the part  $1 - \alpha$  is undissociated. If this is present in  $V$  litres, its concentration is  $\frac{1 - \alpha}{V}$ .

Since  $C_{\text{CH}_3\text{COOH}}$  represents this concentration of the undissociated part in our equation (2),  $C_{\text{CH}_3\text{COOH}} = \frac{1-\alpha}{V}$ ; similarly the concentration of the dissociated part is  $\frac{\alpha}{V}$ ; and since  $C_{\text{H}}$  in the equation (2) represents this undissociated part,  $C_{\text{H}} = \frac{\alpha}{V}$ , wherefore  $C^2_{\text{H}} = \frac{\alpha^2}{V^2}$ .

If now we write the values of  $C^2_{\text{H}}$  and  $C_{\text{CH}_3\text{COOH}}$  into equation (2), then

$$K = \frac{\frac{\alpha^2}{V^2}}{\frac{1-\alpha}{V}} = \frac{\alpha^2}{V(1-\alpha)}, \quad (5)$$

or

$$KV = \frac{\alpha^2}{1-\alpha}. \quad (6)$$

If, therefore, the concentration ( $V$ ) and the dissociation constant ( $K$ ) of acetic acid are known, we can calculate the degree of dissociation ( $\alpha$ ) for this concentration ( $V$ ).

For reasons to be discussed later on, the dissociation constant is often called the *affinity constant*.

The significance of this constant becomes intelligible when we answer the question: How great is  $K$  when  $\alpha = \frac{1}{2}$ , that is to say, when the dissolved substance is dissociated one half? Under these circumstances we find that

$$K = \frac{(\frac{1}{2})^2}{V(1-\frac{1}{2})}, \quad \text{or} \quad 2K = \frac{1}{V}.$$

Twice the value of the dissociation constant is therefore equal to the reciprocal value of the volume at which the dissolved electrolyte is just one half dissociated.

If we determine the relation that exists between the dissociated and the undissociated part of the dissolved electrolyte, at various concentrations (that is to say, when  $V$  has

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various values), we shall obtain, according to equation (5) or (6), a constant value  $K$  which is connected with the concentration as shown in the equation.

The law represented by equation (6) is known as the *dilution law of Ostwald*.\*

Since, as we have seen before (p. 210), the degree of dissociation ( $\alpha$ ) of an electrolyte can be ascertained by determining  $\Delta_V$  and  $\Delta_\infty$ , we can substitute  $\frac{\Delta_V}{\Delta_\infty}$  for  $\alpha$  in equation (5) and so find that

$$K = \frac{\left(\frac{\Delta_V}{\Delta_\infty}\right)}{V \left(1 - \frac{\Delta_V}{\Delta_\infty}\right)}. \quad (7)$$

As a matter of fact, Ostwald, by determining  $\Delta_V$  and  $\Delta_\infty$  of several hundred organic acids, has been able to confirm equation (7) by experiment. As examples from an enormous number of data, I give here the results of measurements made at 25° upon acetic acid (Ostwald †) and ammonia (Bredig ‡):

ACETIC ACID.

$V$	$\alpha$	$K$
8	0.01193	0.0000180
16	0.01673	179
32	0.02380	182
64	0.0333	179
128	0.0468	179
256	0.0656	180
512	0.0914	180
1024	0.1266	178

AMMONIA.

$V$	$\alpha$	$K$
8	0.0135	0.000023
16	0.0188	23
32	0.0265	23
64	0.0376	23
128	0.0533	23
256	0.0754	24

Under  $V$  is given the number of litres in which one mol of the electrolyte is dissolved, under  $\alpha$  the degree of dissocia-

\* Ostwald, *Zeitschr. f. physik. Chem.* 2, 36 (1888).

† *Ibid.* 3, 170, 241, 369 (1889).

‡ *Ibid.* 13, 289 (1894).

tion as calculated from the electrical conductivity, under  $K$  the constants as calculated by equation (7).

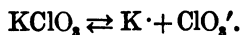
I would especially emphasise that the dilution law of Ostwald, according to present observations, holds only for weakly dissociated electrolytes, such as the organic acids and the weak inorganic and organic bases. Acids, bases, and neutral salts which are greatly dissociated—such, for example, as HCl, NaOH, NaCl, etc.—do not obey this law. The reason for this deviation has not yet been discovered.

I would now like to direct your attention to a second highly important analogy that exists between electrolytic dissociation and the dissociation of dilute gases.

When hydriodic acid, for example, is contained in a given space and dissociation has occurred, we know (see pp. 77 and 78) that the addition of a neutral gas has no effect upon the dissociation equilibrium, but that the addition of one of the dissociation products, either  $I_2$  or  $H_2$ , decreases the dissociation.

If now we imagine a saturated aqueous solution of an electrolyte, such as  $KClO_3$ , which has in part split into its ions  $K$  and  $ClO_3$ , then the question arises: What will happen if we add one of the dissociation products, either  $K$  or  $ClO_3$  ions, to this solution?

If the temperature is constant, then the concentration of the dissolved  $KClO_3$  is also constant, and the following equilibrium prevails in the solution:



If we make use of the Guldberg-Waage law, we find that

$$k_1 C_{KClO_3} = k_2 C_K \times C_{ClO_3}.$$

$k_1$  is here the velocity with which the undissociated salt splits into its ions,  $k_2$  that with which the ions again build up the undissociated salt.

Now

$$\frac{k_1}{k_2} = K = \frac{C_K \times C_{ClO_3}}{C_{KClO_3}}.$$

Since  $C_{KClO_3}$  is constant in the saturated  $KClO_3$  solution, we can substitute a new constant  $K_1$  for the value  $K \times C_{ClO_3}$ , wherefore

$$K_1 = C_K \times C_{ClO_3}.$$

In words: the product of the ion concentrations in the solution (*solubility product*) is constant.

If now we increase the value of  $C_K$  (or  $C_{ClO_3}$ ) by the addition of K ions (or  $ClO_3$  ions), then, since the value of  $K_1$  always remains constant,  $C_{ClO_3}$  (or  $C_K$ ) must correspondingly diminish. This can come to pass only if a part of the ions are reconverted into undissociated  $KClO_3$  molecules. These will then separate out as a solid, for  $C_{KClO_3}$  can also not rise above its constant value.

So, then, just as the dissociation of a dilute dissociated gas is decreased if, at constant volume, one of the dissociation products is added, so the dissociation of an electrolyte is diminished if (at constant volume) one of its ions is added to its solution.

Since it is impossible to introduce free ions as such into a solution, we use the solution of an electrolyte which has an ion in common with  $KClO_3$ , as, for example,  $KCl$  or  $NaClO_3$ . In the aqueous  $KCl$  solution are found free  $K^+$  and  $Cl^-$  ions, while in the  $NaClO_3$  solution are found free  $Na^+$  and  $ClO_3^-$  ions.

If, therefore, we add either a solution of  $\text{KCl}$  or  $\text{NaClO}_3$  to the  $\text{KClO}_3$  solution, crystals of  $\text{KClO}_3$  ought to separate out. Experiment, indeed, shows this to be the case. Advantage is often taken of this fact in the arts; so, for example, crystallised sodium chloride will separate from a saturated sodium chloride solution if free  $\text{Cl}$  ions in the form of  $\text{HCl}$ , for example, are added to the solution.

For this theory of the *depression of solubility* which explains also quantitatively the phenomena that fall under this heading, we are indebted to Nernst.\*

In the foregoing we have shown the importance of the ionic theory in the explanation of the exceptions shown by dilute solutions to the simple laws of osmotic pressure. We shall now consider its influence upon the development of our chemical conceptions.

Since electrolytes in dilute solution are for the most part dissociated into their constituent ions, and since these conduct themselves as independent molecules, the properties of such solutions must be determined not by the properties of the dissolved substances as such, but by the properties of the ions that these molecules yield. We can express this idea also in the following way: The properties of the solution of a highly dissociated substance are *additive*; they are equal to the sum of the properties of the ions which are present in this solution. A solution in which the electrolyte silver nitrate, which dissociates into its ions  $\text{Ag}^+$  and  $\text{NO}_3^-$ , is dissolved, will consequently show the properties that characterise the  $\text{Ag}$  ion and the  $\text{NO}_3$  ion. We must also expect that if silver ions are present in a solution, this solution will possess the properties characteristic of the  $\text{Ag}$  ion,

\* Zeitschr. f. physik. Chem. 4, 372 (1889).

independently of the fact whether this ion originated from dissolved silver sulphate or silver nitrate.

Such a solution, for example, yields a precipitate of silver chloride with an aqueous HCl solution, because the silver ion forms insoluble silver chloride with the chlorine ion found in the aqueous hydrochloric acid solution. When we see that no precipitate of silver chloride is formed in a solution of potassium chlorate when a solution containing silver ions is added, we may conclude that no chlorine ions are present in the potassium chlorate solution, for silver ions always yield silver chloride when they come in contact with chlorine ions.

Examination indeed shows that potassium chlorate forms not chlorine ions, but  $\text{ClO}_3$  ions when it dissociates, and these of course cannot form silver chloride with the silver ions.

If, as is usually the case, fairly concentrated solutions are employed, the solutions contain undissociated molecules as well as ions. If now a reaction takes place between two or more dissolved substances, the question arises, Is it between the molecules or between the ions that the reaction occurs? According to our present knowledge, this question is to be answered by the statement, that the most, if not all, chemical reactions are ion reactions.

If dry hydrochloric acid is dissolved in dry chloroform, a solution is obtained which does not conduct the electric current. There are therefore no ions present in this solution. If this solution is brought in contact with a carbonate, the carbonate is not decomposed. Yet a trace of water suffices to bring about the dissociation of the HCl, and as soon as this is accomplished the chemical reaction also



takes place. The molecules as such therefore do not react with each other.

In view of the importance of these facts in the theory of disinfection, I wish to point out the difference between the so-called *double salts* and *complex salts*. If, for example, copper sulphate ( $\text{CuSO}_4$ ) and potassium sulphate ( $\text{K}_2\text{SO}_4$ ) are dissolved in water, and the two solutions are mixed, a salt crystallises from this solution upon cooling to which the name potassium copper sulphate has been given, and which can be represented by the formula  $\text{CuSO}_4 \cdot \text{K}_2\text{SO}_4 \cdot 6\text{H}_2\text{O}$ .

If this salt is redissolved in water, copper ions (by means of  $\text{H}_2\text{S}$ ), potassium ions (by means of  $\text{H}_2\text{PtCl}_6$ ), and sulphate ions (by means of  $\text{BaCl}_2$ ) can be proved to exist in the solution. Now the salt  $\text{CuSO}_4 \cdot \text{K}_2\text{SO}_4 \cdot 6\text{H}_2\text{O}$  is called a *double salt*; such a salt gives in solution the reactions which the ions entering into its composition give. The depression of the freezing-point of the solution of a double salt is equal to the sum of the freezing-point depressions of its components ( $\text{CuSO}_4$  and  $\text{K}_2\text{SO}_4$ ).

Upon the other hand, if we deal with the solution of such a salt as potassium silver cyanide, formed by dissolving silver cyanide in potassium cyanide, we find, for example, that no precipitate of silver chloride is produced upon the addition of a chloride. There are therefore no silver ions present in the potassium silver cyanide solution. Now experiment has shown that this salt dissociates into the ions  $\text{K}$  and  $\text{Ag}(\text{CN})_2$ . Such a salt is known as a *complex salt*; the properties of its components have not remained unaltered, and the ions present in the solutions of its components ( $\text{K}$ ,  $\text{CN}$ ,  $\text{Ag}$ ) cannot be found unchanged in the solution of the complex salt. This explains why the depres-

sion of the freezing-point of a solution of such a complex salt is not equal to the sum of the freezing-point depressions given by each of the components.

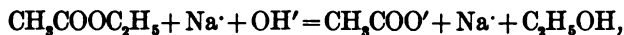
By these and similar considerations the basis of analytical chemistry, which deals with the reactions that occur between ions, is not only much simplified but an unforced explanation is given of countless facts that have long been known.\*

In considering the saponification of ethyl acetate by sodium hydroxide (cf. p. 19) it was pointed out that the velocity with which this reaction occurs at a certain temperature is the same whether we employ NaOH, KOH, or Ba(OH)<sub>2</sub>.

If we view the reaction in the light of the theory of electrolytic dissociation, this fact is readily explained.

Ethyl acetate, even in aqueous solution, does not conduct the electric current, hence it is a non-electrolyte; there are, therefore, no ions, but only molecules of this substance present in the solution. Upon the other hand, sodium hydroxide, in dilute aqueous solution, is dissociated into its ions Na' and OH'.

The course of the saponification may therefore be represented by the following equation

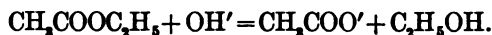


for as we have shown, sodium acetate in aqueous solution is also dissociated into its ions.

Now since the Na ion appears upon both sides of the sign

\* See Ostwald, *The Scientific Foundations of Analytical Chemistry*. Trans. by George McGowan, London and New York 1895 (Macmillan). Abegg u. Herz, *Chemisches Praktikum*, Göttingen 1900.

of equality, it may be omitted. Our equation then assumes the following form:



The metallic ion (cation) which was originally united to the hydroxyl (OH) ion consequently plays no part. It is the hydroxyl ions that bring about the saponification. The velocity with which the saponification occurs will depend, it is evident, *ceteris paribus*, upon the concentration of these ions, that is to say, upon the number of them in the unit volume. Now the concentration of the hydroxyl ions in the solution of a certain base (for example, NaOH) is dependent upon the degree of dissociation of the dissolved substance, for as this becomes greater the number of OH ions in the unit volume of the solution also becomes greater. It can, therefore, be easily understood why such bases as NaOH, KOH, and Ba(OH)<sub>2</sub>, which at the same concentration are equally dissociated, and consequently contain the same number of OH ions per unit volume, should bring about saponification, as experiment has shown, with the same velocity.

Conversely, a base such as NH<sub>4</sub>OH, which at the same concentration is less dissociated than NaOH, will saponify more slowly.

The phenomena observed in the inversion of cane-sugar (see p. 20) under the catalytic influence of dilute acids can also be explained in this way. We have seen that the inverting action of acids is to be attributed to the hydrogen ions they contain. Those acids which are most highly dissociated, that is, those which in solution contain the largest number of hydrogen ions per unit volume, consequently invert most rapidly. Indeed we are already acquainted

with the fact that in very dilute solutions the inversion velocity is directly proportional to the number of free hydrogen ions (see p. 28). Similar facts underlie the catalysis of methyl acetate by dilute acids (cf. p. 32).

If solutions of different acids are prepared containing the same number of mols per litre, then the number of hydrogen ions in a definite volume of these solutions will be greater in those acids which are strongly dissociated than in those in which the dissociation is less; the former acids are called stronger than the latter. As is evident from the foregoing, they show their greater strength (affinity) in that they invert (catalyse) more quickly than the weak acids. The inversion method consequently becomes a means of comparing the strengths of various acids with each other.

The table upon p. 27 which gives the inversion velocity of cane-sugar at 25° under the influence of various acids (of the same concentration,  $\frac{1}{2}$  N), and in which the inversion velocity of hydrochloric acid is taken as unity, shows that hydrochloric acid has the same strength as nitric acid, but that acetic acid, at this concentration, is about 250 times weaker.

Yet I would especially emphasise the fact that with increasing dilution the strengths of the various acids become more and more nearly equal; at very great (infinite) dilution all acids are of the same strength. Though originally, for example, a mol of hydrochloric acid and a mol of acetic acid were each present in a litre of water, yet, when the dilution is very high and dissociation in consequence is complete, equal volumes of the dilute solutions will contain the same number of hydrogen ions. In other words, the acids will have become of the same strength.

The same reasoning, of course, holds for bases also.

Since the equation

$$K = \frac{\alpha^2}{V(1-\alpha)}$$

shows the relation that exists between the degree of dissociation (consequently also the number of free ions) and the dilution, and since the affinity of a dissolved substance is dependent upon the number of ions contained in a definite volume, the constant  $K$  has been called the *affinity constant*.

If we, therefore, say that the affinity constant of a certain acid is greater than that of another acid, the first is stronger than the second, and behaves in its reactions more like an acid than the other, the affinity constant of which has a lesser value.

The affinity constant ( $K$ ) of a number of substances at 25° is given in the following table:

Acetic acid.....	0.0000180
Monochloracetic acid.....	0.00155
Dichloracetic acid .....	0.0514
Trichloracetic acid.....	1.21

We see from this table that as chlorine atoms are substituted for the hydrogen atoms in the acetic acid, acids are formed which are stronger than the acetic acid itself.

It also at once becomes apparent from the above table that the trichloracetic acid will invert cane-sugar more rapidly than acetic acid, and in general in proportion as its acidity is greater than that of its mother substance. The affinity constants consequently give us the chemical characteristics of the substance along the line to which they refer.

In conclusion we shall cast a passing glance upon

*The Electrolytic Dissociation Water, and Hydrolysis.*

Until now we have presupposed in our discussions that pure water is a non-electrolyte, a substance which does not at all conduct the electric current.

When we once before (see p. 217) spoke of the conductivity of water, we referred only to the conductivity observed because of the impurities (traces of electrolytes) present in even very pure water.

But the very carefully conducted investigations of Kohlrausch and Heydweiller \* have shown that even the purest water is electrolytically dissociated, though only very slightly.

Concerning the conductivity of the purest water that has ever been produced, Kohlrausch and Heydweiller have the following to say: "1 mm. of this water has at 0° a resistance equal to that of a copper wire of the same cross-section 40 million kilometres long, a wire that could therefore be wound a thousand times around the earth. This much can further be accepted as probably true (from what is to be said later on) *that this water is the purest that has ever existed*, whether artificially prepared or ready formed in nature; even the precipitations floating highest in the atmosphere scarcely excepted. Simple contact with the air for a short time raised the conductivity of our water tenfold. The impurities still present in the water may be estimated as a few thousandths of a milligram per litre."

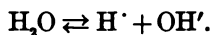
If from these data the degree of dissociation of this water is calculated, it is found that at 18° about 1 mol (18 g.) of

\* See Kohlrausch and Holborn, *Das Leitvermögen der Elektrolyte*. Leipzig 1898, p. 111. Poggendorfs Ann., *Ergänzungsband* 8, 1 (1876). Wiedemanns Ann. 24, 48 (1884); *ibid.* 44, 577 (1891). Ber. d. d. chem. Ges. 26, 2998 (1893). Wiedemanns Ann. 53, 209 (1894). Zeitschr. f. physik. Chem 14, 370 (1894).

water in 12.5 million litres is dissociated into its ions, H<sup>+</sup> and OH<sup>-</sup>.

Of great importance is the fact that Ostwald,\* Arrhenius,† Bredig,‡ and Wijs § have come to the same conclusion upon totally different grounds.

Dissociation occurs according to the formula



We may conclude from this that water can conduct itself either as an acid (since there are free hydrogen ions present in it) or as a base (since OH ions are present).

The knowledge that water is electrolytically dissociated, even though only to an exceedingly small amount, is of great importance in the explanation of a group of phenomena which have long been classed under the name of *hydrolysis*.

In methyl acetate (cf. p. 32) we have become acquainted with a substance that is dissociated into its components, acid and alcohol, by water, yet many salts also have this property. In general, the statement can be made that all salts are decomposed by water into acids and bases, yet the hydrolysis is in most cases so slight that it cannot be discovered with the analytical means at our disposal. This is the case, for example, when we dissolve the salt of a strong base with a strong acid (such as NaCl) in water.

Hydrolysis can, however, be clearly demonstrated when we deal with the action of water upon such a salt as KCN, which is formed by the action of a weak acid upon a strong

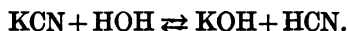
\* Zeitschr. f. physik. Chem. 11, 521 (1893).

† Ibid. 11, 827 (1893).

‡ Ibid. 11, 829 (1893).

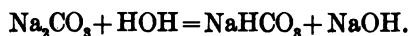
§ Ibid. 11, 429 (1893); 12, 514 (1893).

base. If we determine the reaction of such a solution of KCN we find that it is strongly alkaline, even though equivalent amounts of alkali and prussic acid are present side by side. We may, therefore, assume that, because of the dissociation of the water, the following reaction has taken place:



That the solution in spite of this is still alkaline in reaction is explained by the fact that, even though the alkali and the acid are both dissociated in the solution, yet the number of OH ions is very great, since KOH dissociates entirely into its ions even at slight dilution, while the prussic acid, a weak acid, because of its slight dissociation yields only a few H ions. There is in consequence a large excess of hydroxyl ions present, and these give to the solution its strongly alkaline reaction.

An entirely analogous explanation can be given for the fact that a watery solution of sodium carbonate is alkaline in reaction. What occurs here is the following:

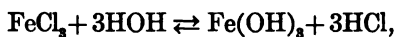


The sodium hydroxide is strongly dissociated, and consequently yields many hydroxyl ions, while the acid salt, sodium bicarbonate, yields almost no hydrogen ions. The excess of hydroxyl ions gives the alkaline reaction to the solution.

The alkaline reaction of soap solutions, which is due to the hydrolytic splitting of the soaps (which, as you know, are alkaline salts of the weak fatty acids, stearic and palmitic acids) by the water, finds in this way an unforced explanation.



If the salt of a strong acid and a weak base, such as ferric chloride ( $\text{FeCl}_3$ ) is dissolved in water, the following reaction takes place,



and the resulting solution, in consequence of the large excess of hydrogen ions originating from the strongly dissociated hydrochloric acid, shows an acid reaction.

I cannot here enter into a description of the methods by which the amount of hydrolysis can be determined, and so content myself with pointing out that in many cases the inversion method or the saponification method yields excellent results.\*

\* See Will and Bredig, *Ber. d. d. chem. Ges.* **21**, 2777 (1888). Walker, *Zeitschr. f. physik. Chem.* **4**, 319 (1889). Shields, *ibid.* **12**, 167 (1893). Koelichen, *ibid.* **33**, 129 (1900). Osaka, *ibid.* **35**, 661 (1900).

## THIRTEENTH LECTURE.

### Applications.

HAVING become acquainted with a number of physico-chemical principles and methods in the preceding lectures, we shall now consider several important problems in the study of which these methods have been employed.

A direct application of the determination of the depression of the freezing-point and of the determination of the conductivity of dilute solutions is found in

#### A. THE FIELD OF HYGIENE,

where, for example, we deal with the examination of certain articles of food, such as milk,\* wine and beer,† or sugar.‡ Yet in these cases the physico-chemical procedures employed assume a certain importance only when they are made in addition to the purely chemical analysis.

In the comparative study of different spring and mineral waters as to the amount of salts they contain,

\* Dohrmann, *Vierteljahresschrift der Forschungen der Chemie der Nahrungs- und Genussmittel* 1891, 1, 13. Thörner, *Chemiker-Zeitung* 1891, 1673. E. Jordis, *Dissertation*, Erlangen 1894. E. Beckmann, *Forschungsberichte über Lebensmittel* 1895, 367. J. Winter, *Compt. rend.* 121, 696 (1895); *ibid.* 123, 1298 (1896). Bordas and Génin, *ibid.* 123, 425 (1896). van der Laan, *Dissertation*. Utrecht 1896.

† E. Beckmann, *l. c.*

‡ Reichert, *Zeitschr. f. anal. Chem.* 28, 14 (1889). Fock, *ibid.* 29, 36 (1890). Arrhenius, *Zeitschr. f. physik. Chem.* 9, 509 (1892).

the determination of the electrical conductivity furnishes a convenient means of attaining our end. *Ceteris paribus*, the conductivity (of waters that do not contain too large an amount of salt) is proportional to the amount of salt they contain.\*

Of very great interest both practically and theoretically are the investigations of Paul and Krönig. †

DISINFECTION IN THE LIGHT OF THE THEORY OF ELECTROLYTIC DISSOCIATION.

These authors studied the germicidal action of various salts, bases, and acids, halogens, oxidising substances, and several organic compounds in aqueous, alcoholic, and ethereal solutions of various concentrations. In all the experiments the temperature was kept constant, since only under such conditions can comparable results be obtained. We have already seen from the observations of Koch, Henle, Pane, and Heider (see p. 66) that the disinfectant action of a solution increases when the temperature is increased. As subjects for experiments, Paul and Krönig used most commonly anthrax spores (*Bacillus*

\* See Kohlrausch and Holborn, *Leitvermögen der Elektrolyte*, Leipzig 1898, and the applications to the field of hygiene by v. d. Plaats, *Verslag omtrent de Verrichtingen van de Gezondheidscommissie der Gemeente Utrecht 1900*, 49. P. Th. Müller, *Compt. rend.* **132**, 1046 (1901).

† *Zeitschr. f. Hygiene und Infektionskrankheiten* **25**, 1 (1897), and *Zeitschr. f. physik. Chem.* **21**, 414 (1896). See also Paul, *Zeitschr. f. angewandte Chem.* **14**, 333. The same: *Entwurf zur einheitlichen Bestimmung chemischer Desinfektionsmittel*, Berlin 1901. Paul and Sarwey: *Experimentaluntersuchungen über Händedesinfektion*, *Münchener mediz. Wochenschr.* No. 49, 51 (1899); No. 27-31 (1900); No. 12 (1901) and *Centralbl. f. Gynäkol.* No. 42 and 49 (1900). Cited from reprints.

*anthracis*) or *Staphylococcus pyogenes aureus*. The germicidal agent employed always acted upon as nearly as possible an equal number of spores, so that the number of bacteria living at the end of an experiment permitted one to judge directly of the disinfecting strength. Bohemian garnets, after being cleaned by boiling in dilute hydrochloric acid, and rinsing in absolute alcohol, were sterilised by heating to 200° C. They were then shaken with an emulsion of the anthrax spores. This emulsion was prepared by rubbing together the agar-agar upon which the cultures grew with water. After the garnets were covered with a certain amount of this emulsion, they were dried at 7° for twelve hours, and stored in an ice-chest. Preliminary experiments had shown that an equal number of spores\* remain attached to each of the garnets prepared in this way. The experiment was then made as follows: Thirty garnets were placed in each of a number of platinum sieves and hung in the germicidal solutions. The latter were contained in glass dishes (with ground covers) kept in a thermostat at 18°.

After the solution had acted for a certain time, the action of the germicidal agent was stopped (according to Gerpert's method), by rinsing the garnets in water and treating them with such reagents as converted the germicidal substances into neutral, non-germicidal substances. So, for example, the salts of the heavy metals were precipitated by a four per cent ammonium sulphide solution; acids and bases were neutralised, etc.

After again washing in water, five garnets each were

\* Those who are acquainted with the method of bacteriology will understand how the phrase "equal number" is to be interpreted.

introduced into test-tubes containing 3 c.c. of water. The tubes were shaken for three minutes, whereby the spores were detached from the garnets and distributed through the water.

The emulsion of spores prepared in this way was heated to 37.5° and added, with stirring, to 10 c.c. of liquid agar-agar solution of 42°. This mixture was then poured into Petri dishes.

The plates remained in the incubator at 37° for three days. After twenty-four hours the colonies were counted for the first time, after seventy-two hours for the last time.

It was found, *ceteris paribus*, that the number of colonies that develop upon a plate is dependent upon the length of the exposure to the germicidal agent, and upon the concentration of the solution used. The number of colonies that develop after a definite length of exposure to a definite concentration of the solution therefore serves as an index of the disinfecting power of the solution under investigation.

It must be noted that by the concentration is always meant the number of mols of dissolved substance contained in the litre, and not the percentage of substance present.

It is of course impossible to describe here the interesting results of these experiments in detail; yet I wish to dwell upon a few of the most important points.

If we remember that an electrolyte in solution is dissociated into its ions only in part, when the solution is not infinitely dilute, then the effect of this solution must be attributed to the combined action of the ions and the undissociated molecules present in it. Paul and Krönig investigated first of all the rôle played by the ions and the undissociated molecules in the disinfectant solutions. For

this purpose the germicidal power of several mercury compounds which are dissociated to different degrees in aqueous solution was examined.

The following short table gives the names of a few of these compounds, arranged in the order of their decreasing degree of dissociation:

1. Mercuric chloride,  $\text{HgCl}_2$ .
2. Mercuric bromide,  $\text{HgBr}_2$ .
3. Mercuric cyanide,  $\text{Hg}(\text{CN})_2$ .

If the germicidal action of the halogen ions (Cl, Br, or CN ions) and the undissociated molecules is slight as compared with that of the Hg ions, then the disinfectant action of these solutions will be dependent in the main upon the concentration of the Hg ions, that is, upon the degree of dissociation of these salts. That this is indeed the case is shown by the following table, which gives the experimental results with *Bacillus anthracis*:

Solution.	20 minutes.	85 minutes.
$\text{HgCl}_2$ , .64 litres .....	7 colonies	0 colonies
$\text{HgBr}_2$ , .64 " .....	34 "	0 "
$\text{Hg}(\text{CN})_2$ , .16 " .....	$\infty$ "	33 "

$\text{HgCl}_2$ , 64 litre means that 64 litres of the solution contain one mol (=271 g.)  $\text{HgCl}_2$ .

It is therefore found that while no more colonies develop after the chloride or the bromide solution has acted for eighty-five minutes, thirty-three colonies can yet develop when a cyanide solution of four times this concentration has acted upon the bacteria for the same length of time.

The results obtained with *Staphylococcus pyogenes aureus* were found to be in harmony with the above:

Solution.	3 minutes.
$\text{HgCl}_2$ , .64 litres .....	0 colonies
$\text{Hg}(\text{CN})_2$ , .16 " .....	6700 "

We may conclude from these experiments that the greater the dissociation of the mercury compound, that is to say, the greater the number of mercury ions present in the unit volume of the given solution, the greater is its disinfectant action. Similar results were obtained by Paul and Krönig with silver, gold, and copper salts.

We have already seen that the degree of dissociation of a dissolved electrolyte is diminished when an electrolyte containing a common ion is added to its solution (p. 224). If the germicidal action of mercury salts is indeed to be attributed to the presence of mercury ions, then the addition of every substance that depresses the degree of dissociation of the dissolved salt must lead to a corresponding depression of the disinfectant action of this solution.

The correctness of this conclusion was proven by Paul and Krönig by adding chlorine ions (such as a NaCl solution) to the sublimate solution and determining the disinfectant action of the resulting solution. The following table gives the measurements made in this direction upon *Bacillus anthracis*:

Solution.	16 litres.		64 litres.		256 litres.	
	12 min.	20 min.	12 min.	20 min.	20 min.	30 min.
HgCl <sub>2</sub> . . . . .	0 col.	0 col.	13 col.	3 col.	56 col.	10 col.
HgCl <sub>2</sub> + 2NaCl . .	3 "	0 "	17 "	5 "	61 "	13 "
HgCl <sub>2</sub> + 4.6NaCl (German Pharmacopœia) . . .	43 "	5 "	34 "	8 "	64 "	14 "
HgCl <sub>2</sub> + 10NaCl	469 "	328 "	103 "	42 "	120 "	16 "

These experiments are also of practical importance. We see from the table that the addition of sodium chloride, especially to the concentrated solutions of the sublimate, lowers its germicidal power. In the dilute solutions (256

litres) the disinfectant action is independent of the addition of the sodium chloride.

All physicians use sublimate pastilles which, to increase their solubility, contain a certain amount of sodium chloride. The German Pharmacopœia (1901) directs: "From a mixture of equal parts of finely powdered mercuric chloride and sodium chloride, dyed red with an aniline dye, are made cylinders weighing one or two grams, each of which is twice as long as it is thick," which about corresponds in composition to  $\text{HgCl}_2 + 4.6\text{NaCl}$ .

In the concentrations in which these are used in practice (1 g.  $\text{HgCl}_2$  per litre, which is about 1 mol  $\text{HgCl}_2$  in 256 litres) the decrease in the germicidal action from the addition of the sodium chloride has almost disappeared; in other words, at this dilution the sodium chloride exerts scarcely any effect upon the disinfectant power of the solution.

It is best not to add more sodium chloride to the sublimate than 2 mols  $\text{NaCl}$  to 1 mol  $\text{HgCl}_2$ . When this amount is exceeded a complex salt ( $\text{Na}_2\text{HgCl}_4$ ) is formed, and we know that in the solution of this salt the mercury ion is no longer present as such. The disinfectant action of the solution would in consequence disappear for the most part.

In accord with the demands of theory, the chlorine compounds of other metals exert the same influence upon the germicidal action of the sublimate solutions as sodium chloride.

We can therefore say that the disinfectant action of aqueous sublimate solutions is weakened by the addition of the metallic chlorides, a fact attributable to the decrease in the degree of dissociation of the mercury compound.

To show the effect of the anion (or the undissociated part



of the salt) upon the disinfectant power of a solution, a number of salts of the same metal, the degree of dissociation of which is about the same, were examined. The following results were obtained with *Bacillus anthracis*:

Solutions.		60 minutes.
AgNO <sub>3</sub>	20 litres.....	27 colonies
AgClO <sub>3</sub>	20 " .....	42 "
AgClO <sub>4</sub>	20 " .....	219 "
Ag <sub>2</sub> SO <sub>4</sub>	40 " .....	1580 "
AgOOCCH <sub>3</sub> C (Silver acetate)	20 " .....	800 "
AgOO <sub>2</sub> SH <sub>3</sub> C <sub>6</sub> (Silver benzenesulphonate)	20 " .....	1654 "
AgOO <sub>2</sub> S(HO)H <sub>3</sub> C <sub>6</sub> (Silver phenolsulphonate)	20 " .....	1643 "

It is evident that the germicidal powers of these solutions differ. If this power were determined solely by the concentration of the metallic ion, these salts should have the same germicidal power, since they contain an equal number of silver ions in the unit volume of solution. We must therefore conclude that this action depends also upon the concentration of the anions, and perhaps upon that of the undissociated molecules.

The investigation of the germicidal action of acids and bases has also brought many interesting facts to light. A few of the general conclusions drawn by Paul and Krönig from their experiments are the following:

1. The germicidal action of solutions of acids runs parallel to that of their degree of dissociation; that is to say, parallel to the number of hydrogen ions contained in the unit volume of solution.

The anions, and also the undissociated molecules of hydrofluoric (HF), nitric (HNO<sub>3</sub>), and trichloroacetic acid (CCl<sub>3</sub>·COOH), have a specific toxic effect upon bacteria.

This when compared with the germicidal effects of the hydrogen ions becomes insignificant with progressive dilution.

2. The disinfectant action of bases, such as calcium, sodium, lithium, and ammonium hydroxide, runs parallel to the number of free hydroxyl ions contained in the unit volume of solution. Many other interesting conclusions must go unnoticed, nor, I am sorry to say, can I enter into the mathematical treatment of the problem studied by Ikeda,\* the relation between the concentration and the germicidal action of a sublimate solution.

As is the case in every investigation, new problems arise here also. Thus, for example, it has been found that while such salts as corrosive sublimate or silver nitrate when dissolved in absolute methyl or ethyl alcohol have only slight germicidal powers corresponding to the slight dissociation in these media, aqueous solutions of these salts show an increased disinfectant action when a not too large amount of these alcohols is added to them.

Very noteworthy and as yet unexplained is the increase in germicidal power shown by aqueous carbolic acid solutions when sodium chloride is added to them. This fact, first discovered by Scheurlen,† was later exhaustively studied by Wiardi Beckman,‡ Paul and Krönig,§ Scheurlen and Spiro,|| and Spiro and Bruns.¶ The more recent

\* *Zeitschr. f. Hyg. u. Infektionskr.* 25, 1 (1897). See also Bredig and Müller von Berneck, *Zeitschr. f. physik. Chem.* 31, 317 (1899).

† Die Bedeutung des Molekularzustandes der wassergelösten Desinfektionsmittel für ihren Wirkungswert. (Published as manuscript.) Strassburg 1895. Printing-office of M. Dumont-Schauberg.

‡ *Centralblatt für Bakteriologie und Parasitenkunde* 20, 577 (1896)

§ *L. c. and Münch. mediz. Wochenschr.* No. 12, 1897.

|| *Ibid.* No. 4, 1897.

¶ *Arch. f. experiment. Path. u. Pharmakol.* 41, 355 (1899). See

investigations of Paul and Krönig have shown furthermore that the addition of organic salts diminishes the germicidal power of phenol solutions less than the addition of inorganic salts, and that phenol solutions which contain sodium salts disinfect more strongly than those which contain potassium salts.

An interesting field for the pharmacologist is also opened here.\*

#### B. THE FIELD OF PHARMACOLOGY.

Dreser † deserves the credit of being the first to utilise the fruits of physical chemistry in his studies on the pharmacology of mercury.

As is known to you, compounds of mercury are poisonous for the animal economy. Whether compounds are used that contain, besides the mercury, the Cl ion, the NO<sub>3</sub> ion, or any other ion, this poisonous action is always found. From this fact it has been concluded that the toxic effects of mercury salts are attributable to that which all these solutions have in common, namely, the mercury ion.

From this it follows that of two solutions containing the same amount of mercury in solution, that one is the more poisonous which is dissociated the more strongly, for, as the degree of dissociation of the dissolved substance becomes greater, the number of free mercury ions present in a given volume of the solution becomes correspondingly greater. The truth of this assumption has been variously confirmed by the experiments of Dreser, ‡ and it can now be said with also Römer, *Münchener mediz. Wochenschr.* 1898, No. 10, and de Freytag, *Arch. f. Hyg.* 20, 70 (1890).

\* M. H. Fischer, *Butler's Materia Medica and Therapeutics*. Saunders and Co., 1902.

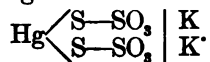
† *Arch. f. Experiment. Path. u. Pharmacol.* 32, 456 (1893).

‡ *Comp. the experiments of Paul and Krönig on p. 236 et seq.*

certainly that the statement of Behring made in 1890, "The antiseptic and disinfectant power of mercury compounds is essentially dependent upon the amount of mercury in solution, it matters not what the name of the compound may be,"\* can no longer stand.

Dreser put yeast-cells into solutions of mercury sulphocyanide and potassium mercury thiosulphate containing the same weight of mercury in solution, and found that while a solution of the sulphocyanide which contained mercury corresponding in amount to a 0.1 per cent sublimate solution prevented the fermentation of sugar by the yeast-cells, this was not the case when the sulphocyanide was replaced by equivalent (and even greater) amounts of the thiosulphate. "The otherwise highly poisonous mercury, in the form of the double thiosulphate, was therefore remarkably non-toxic for the yeast-cells." † This phenomenon is readily intelligible, however, when I remind you of what was said earlier concerning the so-called *complex* salts (see p. 226).

If the potassium mercury thiosulphate [made, for example, by adding yellow mercury oxide (HgO) to a potassium thiosulphate solution (K<sub>2</sub>S<sub>2</sub>O<sub>3</sub>)] is dissolved in water, it dissociates into its ions, as especially arranged experiments have shown, according to the following scheme:



No mercury ions are therefore present in the solution. The ions are K and  $\text{Hg} \begin{array}{l} \diagup \text{S-SO}_3 \\ \diagdown \text{S-SO}_3 \end{array}$ , and the toxic effects that belong to mercury ions in general play no rôle here. We

\* Zeitschr. f. Hyg. 9, 395 (1890).

† Dreser always speaks of a *double salt* in his paper where, as we shall see, he means a *complex salt*. He understood the phenomena with which he dealt, however, from the beginning.

deal here with a *complex* salt that may be considered as the potassium salt of a mercury-thiosulphuric acid, which in water breaks up into the potassium ions and the anions containing the mercury and the remaining part of the molecule.

The difference in the action of equally strong solutions of this salt upon warm-blooded and upon cold-blooded animals is also worthy of note. While the salt first shows its effect upon fishes after a long time, the effect upon rabbits is as great as that of an equally concentrated (with reference to the amount of mercury present) sublimate solution. Evidently the  $\text{Hg} \begin{matrix} \diagup \text{S} - \text{SO}_3 \\ \diagdown \text{S} - \text{SO}_3 \end{matrix}$  ion is rapidly decomposed in the warm-blooded body and mercury ions are formed which then exert their toxic effects.

In passing we may say that the phenomena observed by Scheurlen and Spiro \* in their experiments on the disinfectant action of potassium mercury thiosulphate solutions can also be entirely explained by the complexity of this salt, and that they are exactly analogous to those observed by Paul and Krönig (see p. 240).

That the facts detailed here have a more universal significance is, of course, self-evident. It would be well, for example, to repeat the investigations of Bogoslowsky, † Rouget, ‡ and Gäthgens § on the toxic effects of silver thiosulphate and silver sodium thiosulphate, and those of Samojloff || and Gerschun ¶ on silver glycerrhizinate and

\* Münch. med. Wochenschr. 1897, No. 4.

† Virchows Arch. 46, 409.

‡ Archives de physiologie norm. et de pathologie 5, 333.

§ Universitätsprogramm, Giessen 1890.

|| Arbeiten des Pharmakologischen Instituts in Dorpat 9.

¶ Ibid. 10, 154.

sodium glycerrhizinate and consider the results obtained from our more modern point of view. .

In his *Lectures on Pharmacology* Stokvis\* writes: "It is an established fact—and all investigators are agreed on this point—that the injection of not too small amounts of these silver salts causes the death of frogs and mammals. But differences of opinion at once arise when we deal with the establishment of the lethal dose of silver in the same animal species, or when, while the same experimental methods are used, different silver compounds are employed. Thus Samojloff found the lethal dose for cats to be 14.3 mg. Ag per kilo of body weight when he used the *Hyposulphis argenti*, and nearly double this amount (27.1 mg. Ag) when he used the *Glycyrrhizinas argenti*. Anatomical changes are not demonstrable after such acute fatal intoxications, and the question might therefore arise as to whether the acid constituent is perhaps not the toxic agent. Control experiments, however, have shown that this is not the case, and that the silver itself brings about the poisonous effect."

Could not an explanation of these facts be found by determining the degree of dissociation of the given salts at the concentrations used in the experiments? If, as Stokvis also seems to assume, the silver ion exerts the toxic effects, then it should be found that the *Hyposulphis argenti*, *ceteris paribus*, is dissociated more strongly than the salt of the glycerrhizinic acid, a supposition that it does not seem too hazardous to make.†

The data given by Samojloff must be replaced by others

\* *Leçons de Pharmacothérapie* 2, 364, Paris 1898.

† The possibility that the undissociated part of the salt may also play a certain rôle must also be considered, and at the same time the influence of the diffusion velocity of the salts.

expressed in mols, since only under such conditions can comparable values be obtained.

The very noteworthy observations of W. His, Jr., and Paul \* on the behaviour of uric acid and its salts in solution are of importance not only to physiological chemistry, but also to pharmacology; the false ideas that have long been held concerning the behaviour of these substances have been set aside by these observations, and new questions have in consequence arisen.

It was soon found that the determinations made by the earlier writers on the solubility of uric acid in pure water were incorrect. How far the individual determinations differed from each other is shown in the following table:

Temperature.	Solubility.	Observer.
In the cold	1 : 10000	Prout and Mitscherlich
11°	1 : 1720	Henry †
20	1 : 14800—1 : 15300	Bensch ‡
18.5	1 : 10075	Behrend and Roosen §
20	1 : 16700	Blarez and Denigès
40	1 : 2400	Smale ¶
18	1 : 16300	Nicolaier **

His and Paul determined the solubility of uric acid in pure water at 18° by shaking the acid for some time in the apparatus described in Fig. 13. Since the solutions rapidly decompose at high temperatures, the saturated solution cannot be evaporated, and dry-weight determinations be

\* *Zeitschr. f. physiol. Chemie* 31 and 64 (1900). *Pharmazeutische Zeitung* 1900 (cited from reprints).

† Berzelius, *Lehrbuch. d. Chem.*, translated by Wöhler, 3. Aufl. 9, 409 (1840).

‡ *Liebigs Annalen der Chemie und Pharmazie* 54, 189 (1845).

§ *Ibid.* 251, 250 (1889).

|| *Compt. rend.* 104, 1847 (1887).

¶ *Centralbl. f. Physiol.* 1895. No. 2

\*\* *Zeitschr. f. klin. Med.* 36, 366 (1899).

made. For this reason an accurately weighed amount of uric acid was shaken with an accurately measured amount of water; after saturation had been reached (after about 75 minutes), the undissolved acid was carefully filtered off and dried over sulphuric acid. With various preparations, and in different experiments, it was found that at 18° one part by weight of uric acid dissolves in 39,480 parts of water. There is therefore dissolved in one litre of the saturated solution  $\frac{1}{39.48} = 0.0253$  g. of acid, or, since the molecular weight ( $C_5H_4N_4O_6$ ) is 168.2, one mol in 6640 litres.

These facts again illustrate how difficult it is to make accurate solubility determinations. As the above determinations show very clearly, the solubility of even such a substance as uric acid, which has been in the hands of numerous investigators, was not accurately known.

Widely differing data may be found in physiological literature on the influence which the addition of hydrochloric acid has upon the solubility of uric acid in water. While Rüdél\* and Smale † assume that such an addition increases the solubility, Zabelin ‡ states that it has no effect.

However, from the principles laid down in our earlier lectures, we can foresee what will happen when hydrochloric acid is added to a saturated solution of uric acid; in other words, what influence the former will have upon the solubility of the latter.

\* Archiv f. exp. Path. u. Pharmakol. 30, 496 (1892).

† Centralbl. f. Physiol. 9, No. 12.

‡ Liebig's Annalen der Chemie und Pharmazie, Supplement II, 313 (1863).



In a uric acid solution undissociated uric acid molecules ( $C_5H_4N_4O_3$ ) exist in equilibrium with the ions H and  $C_5H_3N_4O_3$ . According to the law of Guldberg and Waage the following relation exists:

$$k_1 C_u = k_2 C_1 \times C_2.$$

Herein  $C_u$  is the concentration of the undissociated uric acid ions,  $C_1$  that of the  $C_5H_3N_4O_3$  ions, and  $C_2$  the concentration of the H ions, while  $k_1$  represents the velocity with which the undissociated acid splits into its ions, and  $k_2$  the velocity with which the molecules are re-formed.

For this reason

$$\frac{k_1}{k_2} C_u = C_1 \times C_2,$$

or, when we substitute  $K$  for  $\frac{k_1}{k_2}$ ,

$$K C_u = C_1 \times C_2. \quad (1)$$

Herein  $K$  is the affinity (dissociation) constant of the uric acid.

When we add an aqueous solution of hydrochloric acid to a saturated solution of uric acid, we introduce free hydrogen ions into the latter, since hydrochloric acid, being a strong acid, is even in fairly concentrated solutions nearly entirely dissociated into its ions H' and Cl'. If the concentration of the hydrogen ions in the solution of uric acid has been increased by  $\gamma$  through the addition of the hydrochloric acid, then, after equilibrium has again been established, the following equation must hold;

$$K C_u = C_1 (C_2 + \gamma). \quad (2)$$

In equations (1) and (2)  $KC_u$  has the same value since  $K$  is a constant and  $C_u$ , the concentration of the undissociated part of the uric acid dissolved in the saturated solution, also has a constant value.

Equation (2) is correct, however, only if the values which  $C_1$  and  $C_2$  had in equation (1) change; in other words, the degree of dissociation of uric acid will suffer some change through the addition of the hydrochloric acid. What this change is can also be predicted.

$C_1$  is equal to  $C_2$ , and  $\gamma$  as compared with  $C_2$  is very large, for even though only an exceedingly small amount of hydrochloric acid is added, the number of hydrogen ions yielded by this strongly dissociated acid is many times greater than that of the hydrogen ions already present which originate from the weakly dissociated uric acid.  $C_1(C_2 + \gamma)$  can therefore retain the same value ( $KC_u$ ) only when  $C_1$ , the concentration of the uric acid ions, becomes exceedingly small. The addition of hydrochloric acid to the saturated uric acid solution, therefore, decreases the dissociation of the latter. Furthermore, when, in consequence of this decrease, uric acid is re-formed from the uric acid ions (and the corresponding number of H ions) it must separate out, for the solution is already saturated. The addition of hydrochloric acid to the saturated solution of uric acid must therefore decrease its solubility. This could indeed be proved by experiment, for when His and Paul determined the solubility of uric acid (at 18°) in normal hydrochloric acid (36.5 HCl per litre) they found that it had dropped from 1 : 39480 to 1 : 42430.

Since the example cited here is very instructive, and since it can be used to show how the behaviour of the uric acid when hydro-

chloric acid is added to it can be predicted quantitatively by our newer theories, we shall enter somewhat more fully into the mathematics which enable us to do this. We have to deal here with the determination of the value of  $C_1$  when  $\gamma$  is known. The affinity constant of uric acid may be determined by calculation (according to p. 220) from the equation

$$K = \frac{\left(\frac{\Lambda_V}{\Lambda_\infty}\right)^2}{V\left(1 - \frac{\Lambda_V}{\Lambda_\infty}\right)}$$

$\Lambda_V$  is the equivalent conductivity of the saturated uric acid solution at  $18^\circ$ ,  $V$  equals 6640, for solubility experiments have shown that at  $18^\circ$  one gram equivalent of uric acid is present in each 6640 litres of the saturated solution;  $\Lambda_\infty$  is the equivalent conductivity of an infinitely dilute uric acid solution at  $18^\circ$ . The former value ( $\Lambda_V$ ) was found to be 32.24 by His and Paul by the conductivity method of Kohlrausch, while  $\Lambda_\infty$  was calculated to be 339 by a method into the description of which we cannot enter here.

The degree of dissociation of uric acid in saturated solution at  $18^\circ$  is therefore

$$\frac{\Lambda_V}{\Lambda_\infty} = \alpha = \frac{32.24}{339} = 0.095.$$

This figure means that 9.5% of the uric acid is dissociated into its ions,  $C_5H_3N_4O_3$  and H, in this solution.

If now we substitute for  $K$  the value found for  $\frac{\Lambda_V}{\Lambda_\infty}$ , then ( $V = 6640$ )

$$K = \frac{0.095^2}{6640(1 - 0.095)} = 0.00000151.$$

Since we before found the affinity constant of acetic acid to be 0.0000180 (see p. 230), we see that acetic acid is about twelve times as strong as uric acid.

Before we calculate the effect of the addition of hydrochloric acid upon the solubility of uric acid, we shall prove that equation (1) of p. 250 is correct quantitatively also.

We already know the value of  $K$ , so that we now have to determine the values of  $C_u$ ,  $C_1$ , and  $C_2$ .

The concentration of uric acid in saturated solution can be found from the data on solubility. Since one mol of uric acid is con-

tained in 6640 litres (see p. 249), its concentration is  $\frac{1}{6640}$ ; that is to say,  $\frac{1}{6640} = 0.0001506$  mol are present in each litre.

Since the degree of dissociation is 0.095 (see above), the concentration ( $C_1$  and  $C_2$  respectively) of the  $C_6H_3N_4O_8$  ions and of the H ions is equal to  $0.095 \times 0.0001506 = 0.0000143$ , and the concentration of the undissociated part of the acid ( $C_u$ ) is equal to  $0.0001506 - 0.0000143 = 0.0001363$ .

If we write these values into equation (1), we find

$$\begin{aligned} 0.00000151 \times 0.0001363 &= 0.0000143 \times 0.0000143. \\ 2.05 \times 10^{-10} &= 2.06 \times 10^{-10}, \end{aligned}$$

a very satisfactory agreement, therefore.

We shall now answer the question, What will be the value of  $C_1$  when we add to one litre of the saturated (at  $18^\circ$ ) solution of uric acid 36.5 g. hydrochloric acid?

If we determine the value of  $C_1$  in equation (2) on p. 250, we find, since  $C_1 = C_2$ , that

$$\begin{aligned} C_1^2 + C_1\gamma - KC_u &= 0. \\ C_1 &= -\frac{\gamma}{2} \pm \sqrt{\left(\frac{\gamma}{2}\right)^2 + KC_u}, \end{aligned}$$

and it becomes our object to determine the numerical values of  $\gamma$  and  $KC_u$  in this equation.

Now we already know the value of  $KC_u$ ; this value amounts to  $2.05 \times 10^{-10} = 0.000000000205$ . In order to find the value of  $\gamma$ , the concentration of the hydrogen ions in a solution in which are dissolved 36.5 g. (1 mol) hydrochloric acid, we determine  $A_V$  and  $A_\infty$  of this hydrochloric acid solution at  $18^\circ$ , from which we then get the degree of dissociation,  $\alpha = \frac{A_V}{A_\infty}$ . If the determination is made according to Kohlrausch's method, it is found that  $A_V = 301$ ;  $A_\infty = 384$ , wherefore  $\alpha = \frac{301}{384} = 0.78$ . This means that in an aqueous hydrochloric acid solution containing 36.5 g. HCl per litre, 78% of the hydrochloric acid is dissociated into hydrogen and chlorine ions. The concentration  $\gamma$  of these ions therefore amounts to 0.78.

If we substitute these figures in equation (3), then

$$C_1 = -\left(\frac{0.78}{2}\right) \pm \sqrt{\left(\frac{0.78}{2}\right)^2 + 0.000000000205}.$$

While, therefore,  $C_1$  originally had the value 0.0000143, this value was very greatly reduced by the addition of the hydrochloric acid. In other words, by the addition of hydrochloric acid the dissociation of uric acid is enormously diminished. We have already seen that this decrease in dissociation leads to a decrease in the solubility of the uric acid. Since the concentration of the dissociated uric acid is 9.5 per cent of the total acid that has gone into solution (see p. 252), the solubility of the acid is diminished by this amount.

If the solubility in pure water (at 18°) is 1:39480, it therefore falls to 1:43260 in a solution that contains 36.5 g. HCl per litre (normal hydrochloric acid solution). We have already said that His and Paul, experimentally, found the solubility to be 1:42430, which agrees favourably with the above.

Similar considerations lead to the conclusion that the solubility of sodium urate in the blood is diminished by the sodium chloride (which has an ion in common with sodium urate) present in it. So, for example, the solubility of sodium urate is decreased by one half in a sodium chloride solution containing  $\frac{1}{8}$  mol (=0.046%) NaCl per litre.

In general, every sodium salt will bring about this result, for, as we know from what has been said before, the decrease in solubility is due to the presence of the common ion. The addition of sodium bicarbonate will therefore also diminish the solubility of the sodium urate.

This fact is of great practical importance. Stokvis, for example, in his *Lectures on Pharmacology* \* writes: "The property of rendering soluble the crystallised precipitates and concretions of uric acid and the urates is also attributed to the bicarbonate of sodium. But the question as to whether this salt is indeed capable of doing this is still open in spite of the investigations of Pfeiffer, †

\* *Léçons de Pharmacothérapie* 2, 117, Paris 1898.

† *Verhandlungen des Kongresses für innere Medizin* 1886, 44. *Ibid.* 1888, 327.

Posner and Goldenberg."\* And further, "that concretions, renal calculi, existing in the kidneys or the urinary passages can be dissolved by the internal use of sodium bicarbonate is highly improbable, if not impossible."

But the question can be answered *a priori* by utilising the principles of physical chemistry. If it were possible to increase the amount of sodium bicarbonate in the blood, gouty deposits would in consequence be dissolved not more readily, but more *difficultly*.

Just as wrong is the idea that potassium or lithium salts are able to convert the difficultly soluble urates into more readily soluble compounds and so act as *litholytics* or *lithotryptics*.†

If in spite of this fact, as many authors believe, mineral waters containing alkalies or lithium have a beneficial effect in pathological conditions brought about by a deposition of uric-acid-like concretions, this does not contradict the teachings of the ionic theory; it only means that another explanation must be sought for these curative effects than has thus far been given.

Stokvis, for example, attributes the litholytic power of many mineral waters to the increased diuresis and the diminished acidity of the urine which result from the use of these waters. This increased diuresis prevents the deposition of uric acid and urates, "but an actual solution of calculi or of tophi that have formed in the joints does not occur, according to my mind."

What has been said of potassium and lithium salts is true also, according to His and Paul, of piperazin and similar preparations the medicinal effects of which are attributed

\* Zeitschr. f. klin. Med. 13, 580.

† See Paul, Pharmazeutische Zeitung 1900.

to the formation of readily soluble salts of uric acid. The compounds which piperazin forms with uric acid in aqueous solution behave like urates.

About ten years ago Rüdél \* believed that he had found in urea a substance capable of dissolving uric acid and urates. His publications have excited great attention and have led to the treatment of gouty conditions with large amounts of urea.

His and Paul have repeated the measurements of Rüdél, and have found that urea has no effect whatsoever upon the solubility of uric acid or urates, so that a scientific foundation for the urea therapy, based upon the results obtained by Rüdél and followed by many, is now lacking.

Physico-chemical methods will probably play no insignificant rôle in the future, when we wish to judge of the pharmacological (or therapeutic) value of spring (mineral) waters; yet it must be borne in mind that these physico-chemical measurements attain a certain importance only when employed in conjunction with a chemical analysis of these waters.

For example, as the observations of Roth and Strauss,† of Pfeiffer and Sommer,‡ and of Strauss § show, the effect of various mineral waters upon absorption and secretion in the stomach is closely related to the osmotic pressure exerted by the salts dissolved in these waters.

By determining the depression of the freezing-point, it is possible to ascertain the number of molecules plus ions that are present in a given volume of a water, and this quantity

\* Archiv f. experiment. Path. u. Pharm. 30, 469 (1892).

† Zeitschr. f. klin. Med. 37, 144 (1900).

‡ Archiv f. experiment. Path. u. Pharmakol. 43, 93 (1899-1900).

§ Therapeutische Monatshefte 13, 583 (1899).

is a measure of the osmotic pressure of the solution (for we can regard every mineral water as a solution).

Furthermore, by determining the conductivity we have a method of ascertaining the number of free ions, from which, after first determining the depression of the freezing-point, we can discover the number of dissociated molecules. Later, in dealing with an example taken from the field of physiology, we shall discuss this process of *osmotic analysis* \* in greater detail.

Before we leave the field of pharmacology I wish to call your attention very briefly to a few points that are of importance in posology (dosology).†

In the pharmacopœia of the German government ‡ is found a so-called table of maximal doses in which are stated the largest doses of medicinal substances that may be given to adults. "The apothecary may dispense for internal use a medicine containing one of the following named substances, in larger amounts than here indicated only when the larger amount is emphasised by an exclamation-point (!)

\* On the analysis of mineral waters see: Köppe, Bedeutung der Salze als Nahrungsmittel, Giessen 1896; Archiv f. Balneotherapie und Hydrotherapie 1898; Deutsche mediz. Wochenschr. 1898, 624; *ibid.* 1900, No. 32; Therapeutische Monatshefte 14, 1900; Balneologische Centralzeitung, Jan. 21, 1901. Lehnert, Dissertation, Erlangen 1897; Scherk, Archiv f. Balneotherapie und Hydrotherapie 1897; Die freien Ionen und die ungelösten Salzverbindungen in ihrer Wirkung bei Gebrauch von natürlichen Mineralwassertrinkuren, Halle 1898. R. Frenkel, Gazette des Eaux 1899, No. 2083; Duhourcau, Annales de la Société d'hydrologie médicale de Paris 1899; Buchböck, Balneologische Zeitung, August 1899; Kostkewicz, Therapeutische Monatshefte 13, 577 (1899); Brasch, Zeitschr. f. diät. und physik. Therapie, 1900, III, Heft 8. P. Th. Müller, Compt. rend. 132, 1046 (1901).

† See Stokvis, Nederlandsch Tijdschrift voor Geneeskunde 1896, 105.

‡ Editio IV, 431 (1900).



made by the physician. This holds also in dispensing one of these substances in the form of an injection or a suppository."

One of the principles upon which this table is based is that the therapeutic action of the substances named therein is proportional to their weight. This assumption is in itself certainly incorrect,\* and we know, moreover, that the action of a dissolved substance depends to a great extent upon the medium in which it is dissolved (see p. 243).

Thus Binnendijk † found that an aqueous solution of carbolic acid has from one half to one fifth its original effect upon dogs and rabbits, whether employed internally or externally, when 20–30 per cent glycerine is added to it. Hallopeau ‡ made the same observation on the action of tartaric acid. The fact (see p. 243) that the addition of sodium chloride to an aqueous phenol solution greatly increases its germicidal power, while such an addition decreases the activity of sublimate solutions under certain conditions, also shows very forcibly the great importance of the medium in which a drug is dissolved. In all these illustrations the mere statement of a maximal dose has therefore no value whatsoever, and in the pharmacopoeial table under discussion the medium in which the various substances are dissolved is not considered at all.

Extensive reforms based upon physical chemistry are therefore to be hoped for in this field also.

\* See Juckuff, *Versuche zur Auffindung eines Dosierungsgesetzes*, Leipzig 1895.

† Sixième Congrès international des Sciences médicales, Amsterdam II, 370.

‡ *Nouv. remed.* 1893, 91.

## FOURTEENTH LECTURE.

### Applications (Continued).

#### C. TO THE FIELD OF PHYSIOLOGY.

THE very important question, from a physiological standpoint, as to how far proteids such as albumose and anti-peptone combine with hydrochloric acid, sodium hydroxide, or sodium chloride has been exhaustively studied not only by O. Cohnheim,\* but also by Bugarszky and Liebermann,† who used among other methods that of determining the freezing-point.

If hydrochloric acid is dissolved in water, the freezing-point of this solution is lower than that of the pure water. If albumose is added to the solution, the freezing-point will change but little if the hydrochloric acid continues to exist as such in the presence of the albumose. The number of molecules dissolved in a definite volume of the solution will of course rise upon the addition of the albumose, but since the molecular weight of the proteids is exceedingly high, an addition of several grams of albumose will correspond to only a very slight increase in the number of molecules in the solution, and consequently will lower the freezing-point of the solution but little.

If, however, the hydrochloric acid unites with the albumose either wholly or in part, the addition of this proteid will diminish the number of hydrochloric acid molecules

\* See p. 28.

† Pfügers Archiv 72, 51 (1898).

(or ions), and will raise the freezing-point of the original hydrochloric acid solution to a corresponding degree; for after the addition of the albumose fewer molecules (or ions) are present in a definite volume of the solution than before.

We have a means of answering this question by determining the freezing-point of the solution, with the Beckmann apparatus, before and after the addition of the albumose.

Bugarszky and Liebermann determined first of all the freezing-point of proteid solutions containing various amounts of albumose. The following table gives the results of these measurements. Under  $g$  is given the number of grams of albumose dissolved in 100 g. of water; under  $a$ , the depression of the freezing-point of these solutions.\*

ALBUMOSE IN WATER.						
$g$ .....	0.25	0.60	1.	2.	4.	8.
$a$ .....	0.004	0.008	0.013	0.020	0.033	0.060

The depression of the freezing-point of a 0.05 N. aqueous hydrochloric acid solution (which therefore contained  $0.05 \times 36.5$  g. HCl = 1.825 g. HCl per litre) to which were added gradually increasing amounts of albumose, was then measured. In the following table the number of grams of albumose present in each 100 g. water is given under  $g$ , under  $\Delta$  the depression of the freezing-point observed; under  $D$  is indicated the depression of the freezing-point

\* Since albumose is a non-electrolyte, it would be expected that its solutions would, from an osmotic standpoint, conduct themselves as cane-sugar solutions; that is to say, the depression of the freezing-point should be proportional to the concentration of the dissolved albumose. That this is not the case, as the table shows, is to be attributed to the fact that it is very difficult to free albumose of all the dissolved salts. The salts give rise to the observed variations from the calculated freezing-points.

which the given solution would show if the number of molecules and ions originally present therein had been increased in amount by the number of molecules of albumose added.  $D$  is therefore equal to the depression of the freezing-point of the pure hydrochloric acid solution ( $0.186^\circ$ ) + the depression of the freezing-point ( $a$ ) of the albumose solution added to it, as given in the foregoing table.

## ALBUMOSE + 0.05 NORMAL HCl.

$a$	$\Delta$	$D = 0.186 + a$
0.	0.186	0.186
0.25	0.184	0.190
0.50	0.178	0.194
1.00	0.167	0.199
2.00	0.148	0.206
4.00	0.116	0.219
8.00	0.156	0.246

We see from this table that with an increase in the amount of albumose added, the freezing-point of the hydrochloric acid solution progressively rises. Molecules (ions) therefore disappear from the solution; that is to say, complex molecules are formed from the hydrochloric acid and the albumose.

As soon as 4 g. of albumose have been added to the hydrochloric acid, any further addition causes a lowering of the freezing-point, and this in proportion to the amount of albumose added. According to the first table 4 g. albumose give a depression of the freezing-point of  $0.033^\circ$ , while from the second table it is seen that 4 g. albumose lowers the freezing-point of the solution (which already contains 4 g. albumose) by  $(0.156 - 0.116 =) 0.040^\circ$ , a depression, therefore, which, within the limits of experimental error, is proportional to the number of albumose molecules added.

We are consequently led to the same conclusion by the freezing-point method as (see p. 28) by the inversion method,—hydrochloric acid combines with albumose.

Bugarszky and Liebermann have extended their experiments to the combining power of albumose with sodium hydroxide and sodium chloride. Albumin and pepsin behave like albumose in every respect. That sodium chloride does not combine with albumin is shown in the following tables:

ALBUMIN IN WATER.						
<i>g</i> .....	0.2	0.4	0.8	1.6	3.2	6.4
<i>a</i> .....	0.002	0.004	0.006	0.009	0.015	0.022

ALBUMIN + 0.05 NORMAL NaCl.

<i>g</i>	$\Delta$	$D = 0.186 + a$
0.	0.183	0.183
0.4	0.186	0.187
0.8	0.191	0.189
1.6	0.194	0.192
3.2	0.199	0.198
6.4	0.203	0.205

As can be seen from this table, the observed depression of the freezing-point ( $\Delta$ ) is always (within the limits of experimental error) equal to the depression of the freezing-point ( $D$ ), which the solutions should show if the NaCl molecules (+ ions) remained unchanged beside the albumin molecules added to them.

In a similar way it was found that NaOH combines with these proteids.

THE TASTE OF DILUTE SOLUTIONS.

This is a subject that within the last few years has been studied from a physico-chemical standpoint. Since we here deal with a subject most difficult of investigation and one of which we know as yet but little, I wish to direct

your attention to it. Here, more than anywhere else, the coöperation of the physical chemist and the physiologist is to be desired.

As early as 1887 Bailey \* observed that equimolecular solutions of acetic acid and hydrochloric acid are not equally sour, but that the hydrochloric acid solution makes a more intense impression upon the tongue than the acetic acid solution.

Later Kahlenberg † studied the question, In how far is the taste of dilute solutions dependent upon the electrolytic dissociation of the dissolved substances?

If we consider the question in the light of this theory, then the properties of a very dilute solution of an electrolyte must be determined by the sum of the properties of the ions contained in it, for in such a solution the dissolved substance is totally dissociated into its ions.

If we compare, for example, very dilute solutions of sodium chloride and hydrochloric acid, which contain equivalent amounts of NaCl and HCl, then, since the dissolved electrolytes are completely dissociated, the concentration of the chlorine ions is the same in both solutions; the differences between the two solutions lie in the fact that the one contains sodium ions, while the other contains hydrogen ions. The differences in taste (in general, the differences in the properties) of the two solutions are therefore to be attributed to the differences between the properties of the sodium and the hydrogen ions.

Now a hydrochloric acid solution still has a distinctly sour taste at a concentration at which a sodium chloride

\* Proceedings, Kansas Academy of Sciences **11**, 10 (1887).

† Bulletin of the University of Wisconsin No. 25, Science Series Vol. 2, No. 1, 1 (1898).

solution containing an equivalent amount of sodium chloride is entirely tasteless. It follows from this that the taste of such a dilute hydrochloric acid solution is to be attributed to the hydrogen ions contained in it. Since the dilute hydrochloric acid has a sour taste, we must conclude that hydrogen ions have a sour taste.

Thus Kahlenberg found that hydrochloric acid solutions having a concentration of  $\frac{1}{200}$  normal,  $\frac{1}{400}$  normal, or even  $\frac{1}{800}$  normal have a sour taste, while upon further dilution the sour taste disappears. Sodium chloride solutions at a concentration of  $\frac{1}{800}$  normal are entirely tasteless.

If solutions are used that are not entirely dissociated, the additional question as to how far the undissociated molecules contribute to the taste of the solution has to be considered.

From Kahlenberg's experiments the general conclusion may be drawn that aqueous solutions of hydrochloric, sulphuric, hydriodic, and nitric acids can be just distinguished from pure distilled water in  $\frac{1}{800}$  normal solutions. This fact is readily intelligible in the light of the dissociation theory, when we remember that these solutions contain the same number of hydrogen ions (which determine the sour taste) in equal volumes of the solutions, for they are equally strongly dissociated.

In the case of acetic acid, both Kahlenberg\* and Richards† observed several facts that cannot be as readily explained as the above. Thus it was found that a  $\frac{1}{400}$  normal solution of this acid has a just perceptible sour taste. Now such a solution is dissociated about 6 per cent,

\* L. c.

† American Chemical Journal 20, 121 (1898); see also Kastle, *ibid.* 466.

wherefore the concentration of the hydrogen ions in it is  $0.06 \times \frac{1}{200}$  normal =  $\frac{6}{20000}$  normal.

But we have seen above that hydrogen ions give a sour taste only in concentrations of  $\frac{1}{800}$  normal, from which it would be concluded that an acetic acid solution having a concentration of hydrogen ions of only  $\frac{6}{20000}$  normal ought to be tasteless.

In the course of an investigation into the relation between the taste of acid salts and their degree of dissociation, these measurements were corroborated by Kahlenberg.\*

To explain these facts various hypotheses have been suggested by Richards,† Ostwald,‡ and Noyes,§ the substantiation of which by more extensive experiments is, however, still lacking.

That many as yet unknown factors play a rôle in the action of solutions or pure substances upon the sense of taste is shown by the fact that many of the observations of Kahlenberg are at variance with those of Höber and Kiewow,|| who, in part at least, studied the same substances. Since all of these authors conclude, from their experiments with salt solutions, that the taste of every salt is made up of the sum of the tastes of its ions, it seems questionable whether further results are obtainable in this direction without utilising the doctrine of *psychic inhibition*, that is, the general fact that a sensation suffers in intensity through the simultaneous introduction of another sensation, and

\* Journal of Physical Chemistry 4, 33 and 533 (1900).

† Ibid. 207.

‡ Zeitschr. f. physik. Chem. 28, 174 (1899).

§ Journal of the American Chemical Society (Review of American Chemical Research) 22, 73 (1900).

|| Zeitschr. f. physik. Chem. 27, 601 (1898).



is therefore either weakened or entirely crowded out of the realm of consciousness.\*

#### THE OSMOTIC PRESSURE OF ANIMAL FLUIDS.

We are all acquainted with the great importance of osmotic phenomena in the metabolism of animals (and plants). The teachings of physical chemistry with which we have become acquainted in the preceding lectures were early employed to explain many of the life-processes that go on in the organism. We stand here at the beginning of a new epoch in physiology, one which already records many noteworthy contributions.

From the exceedingly rich material at hand permit me to bring a few of the most important facts to your attention.

It has already been pointed out that the actions of various substances upon each other are comparable only when the number of mols that enter into the reaction are taken into consideration. This naturally holds true also when we deal with the processes that go on in the living organism.

To give the concentration of the reacting substances in per cents, as is often done in physiology even to-day, can therefore never yield comparable results. We have already had various illustrations of the truth of this fact. I need but to remind you of the investigations of Hamburger, Massart, Dreser, Paul, and Krönig. To these I add Limbeck,† who determined what concentrations of various salts are necessary to produce diuresis,

\* For specific instances of psychic inhibition, see Heyman's *Untersuchungen über psychische Hemmung*, *Zeitschr. f. Psychologie u. Physiologie der Sinnesorgane* 21, 321 (1899).

† *Archiv f. experiment. Path. u. Pharm.* 25, 69 (1889).

and in whose experiments it was found that the different solutions employed were isotonic. This observation strongly supports the idea that the cells which secrete the urine are stimulated by a change in the osmotic pressure of the blood, and that isotonic salt solutions give rise to stimuli of equal intensity.

While chemical analysis can tell us much concerning the composition of physiological fluids, it cannot yield us anything definite concerning the osmotic behaviour of such solutions. This becomes intelligible when we remember that the osmotic pressure of a solution is dependent upon the number of molecules (+ ions) it contains, and that this cannot be determined by chemical analysis. For when the organic substances present in physiological fluids are incinerated, well-known inorganic acids and salts are formed therefrom by oxidation which, when dissolved in water equal in volume to that of the liquid originally subjected to analysis, produce an osmotic pressure entirely different from that of the substances from which they were formed. So, for example, the proteids originally present, which because of their high molecular weight exert an exceedingly low osmotic pressure, yield certain inorganic substances after incineration which, in consequence of their electrolytic dissociation in aqueous solution show a considerable osmotic pressure.

If, therefore, we wish to become acquainted with the osmotic behaviour of such animal fluids, we must measure their osmotic pressures by methods which leave them entirely unaltered.

By determining the lowering of the freezing-point we have a direct means of accomplishing our end. This method has been employed by many physiologists in the

study of osmotic equilibrium and its influence upon the metabolism of the animal organism.

A general summary of the freezing-point depressions of several important animal fluids, which serve as a measure of their osmotic pressure, is given in the table on p. 269.

To this table must be added the fact that, according to Hamburger's\* experiments, the freezing-point of defibrinated blood is the same as that of serum. In other words, the presence of the blood-corpuscles has no effect upon the freezing-point. This result is intelligible when we remember that proteids, because of their high molecular weight, have an exceedingly low osmotic pressure, and therefore (practically) do not add to the depression of the freezing-point of the blood.

Of importance, too, is the fact, as Hamburger has shown, that the freezing-point of the blood does not change during hemorrhage.†

While Köppe states that the depression of the freezing-point of the serum of coagulated and defibrinated blood is equal to 0.570, he finds that the depression of the freezing-point of the red blood-corpuscle pulp is equal to 0.535. The very careful measurements of Krönig and Fueth,‡ however, have shown that this difference does not really exist, and that the freezing-point of the blood-plasma, or of the blood-serum and blood-corpuscle pulp, is the same. This fact is readily understood when we remember that in the intimate mixture of the blood-corpuscles with the serum

\* *Centralbl. f. Physiol.* 11, 217 (1897)

† *Ibid.* 1895, Heft 6. Cited from a reprint.

‡ *Monatschr. f. Geburtsh. u. Gynäk.* 13, 1-35 (1901). Cited from a reprint.

FREEZING-POINT (DEGREES CENTIGRADE UNDER 0) OF THE BLOOD.\*

Observer.	Man.	Ox.	Calf.	Sheep.	Horse.	Hog.	Chicken.	Dog.	Cat.	Rabbit.
Korányi †	0.56									
Vrinus †	0.528-0.533				0.549		0.617-0.624			
Körppe †	0.508-0.535									
Kosser †	0.54-0.58									
Kimmel †	0.55-0.58									
Kamburger **	0.56	0.600			0.582	0.623		0.602		0.579
Winter †	0.56-0.59	0.57-0.60		0.56-0.58	0.55-0.565	0.55	0.613	0.565		0.57
Koch †	0.58-0.59									
Preser †	0.58-0.59									
Brand †	0.58-0.60									
Bugarzky and Langl †					0.527-0.532	0.588- 0.613		0.570-0.601 0.605 0.633		
König and Fueth **	0.520 (blood of the senile and the new- born)	0.575-0.609						0.583- 0.642 0.57- 0.63		0.61-0.63
Hedin †††										
Heidenhain †††										
Höber †††										

\* Experiments have been made on the osmotic pressure of the blood of marine animals by Bottazzi [Archives italiennes de Biologie 23, 61 (1897)], which show that this pressure is equal to that of the water in which they live. In the higher marine vertebrates the osmotic pressure is entirely independent of that of the medium in which they live.

† Centralbl. f. Physiologie 8, 503 (1894); Zeitschr. f. klin. Medizin 33, 1 (1897); ibid. 34, 1 (1898)

† Physiik Arch. 53, 86 (1896).

‡ Centralbl. f. Physiologie 7, 758 (1894); ibid. 11, 217 (1897).

§ Archives de Physiologie normale et de path. Série 5, 8, 114 (1896).

\*\* Centralbl. f. Physiologie 7, 758 (1894); ibid. 11, 217 (1897).

†† Virchow's Arch. 154, 466 (1890).

††† Arch. f. experim. Path. u. Pharm. 29, 303 (1892).

‡‡ Dissertat. Amsterdam, 1901.

§§ Centralbl. f. Physiologie 1897, No. 9.

¶¶ Monatssehr. f. Geburtsh. u. Gynäk. 13, 1901. Cited from reprint.

‡‡‡ Ibid. 76, 629 (1898).

††† Skandinav. Arch. f. Physiol. 5, 385 (1896).

††† Pflügers Arch. 56, 600 (1894).

‡‡‡ Ibid. 76, 629 (1898).

† La semaine médicale 1900, 142.

an equalisation of the osmotic pressure in the two liquids is to be expected:

The osmotic pressure of many other animal fluids has been examined. The table on p. 271 contains a few data concerning the same.

The figures given in this table have only a relative value, as fluids from different individuals were examined, and in such cases no inconsiderable variations are always found. For this reason we give a series of observations made upon the body fluids of a single individual; these show that osmotic equilibrium exists between the various body fluids (with the exception of the urine).

DEPRESSION OF THE FREEZING-POINT.

Of cow's milk.....	0.570
Of the serum of the same cow.....	0.570
Of the amniotic fluid.....	0.575

The considerable differences that exist between the observations of various authors (see, for example, the table on p. 269) are probably attributable to errors in experimental technique or differences in the instruments used; we shall return to these later, yet it may be said in passing that greater attention should be paid to such mistakes than has thus far been the case in physiology, for these differences in the data obtained imperil the conclusions drawn therefrom.

The great importance in diagnosis of a study of the osmotic behaviour of the blood and of the urine has been shown most clearly by v. Korányi. Korányi's work has been followed by that of many other observers. By determining the freezing-point of the blood and of the urine it is possible to discover a lessened permeability of the

DEPRESSION OF THE FREEZING-POINT.

Observer.	Urine.	Milk.	Saliva.	Bile.	Amniotic Fluid.	Perspiration.
Dreser *		(cow) 0.55-0.57		(cow) 0.54-0.56		
Korányi †	1.3-2.2					
Schaefer †	0.802-1.407					
Bugarszky §	1.187-2.111					
Claude and Balthazard	1.3-2.2		0.10	(human) 0.54-0.58		
Brand ¶						
Hamburger **		(cow) 0.556-0.574				
Köppe ††		(human) 0.495-0.630			(cow) 0.575	
Bordas and Génin ††		(cow) 0.44-0.56			(human) 0.496	
Veit §§					(human) 0.451	
Krönig and Fueth						
Beckmann-Jordis ¶¶		0.554				
Winter ***		0.55-0.57				0.08-0.46
Ardin-Delteil †††						

\* Archiv f. exp. Path. u. Pharmacol. 9, 303 (1892).

† Zeitschr. f. klin. Med. 33, 1 (1897).

‡ Dissertation, Giessen.

§ Pflügers Arch. 68, 389 (1897).

|| La Cryoscopie des Urines, Paris 1901.

¶ Dissertation, Amsterdam 1901.

\*\* Zeitschr. f. Fleisch- u. Milchhygiene 6, 167.

†† Habilitationschrift, Giessen 1898.

‡‡ Compt. rend. 123, 425 (1896).

§§ Zeitschr. f. Geburtshilfe und Gynäkologie 45, 316 (1900).

|| Monatsschr. f. Geburtsh. u. Gynäkol. 13, 1901. Cited from reprint.

¶¶ Forschungsberichte über Lebensmittel 1895, 367.

\*\*\* Compt. rend. 121, 696 (1895).

††† Ibid. 13, 844 (1900).

kidneys for dissolved molecules, and disturbances in the secretion of water.\*

In metabolism the large proteid molecules which in solution exert an exceedingly low osmotic pressure are split into smaller ones. In consequence the number of dissolved molecules in the tissue fluids and in the blood is increased, which causes an increase in the depression of the freezing-point of these fluids. The loss of water by the body through evaporation has a similar effect. It is the function of the kidneys to rid the body of this excessive number of molecules, and so keep the osmotic pressure of the blood and of the other body fluids constant.

If the activity of the kidneys is decreased, the depression of the freezing-point of the blood will become greater. A beginning renal insufficiency will therefore be manifested by an abnormally great depression of the freezing-point of the blood.

\* *Zeitschr. f. klin. Med.* 33, 1 (1897); 34, 1 (1898), where references to the literature may be found; *Pester med. chir. Presse* 34, No. 52, 1898; *Ungarische med. Presse* 1898, No. 13-15; *Berliner klin. Wochenschr.* 1899, No. 5; *ibid.* 1899, No. 36; *Monatsberich. über die Gesamtleistungen auf dem Gebiete der Krankheiten der Harn- und Sexualapparate* 4, No. 1 (1899); *ibid.* 5, No. 5 (1900); *Centralblatt für die Krankheiten der Harn- und Sexualorgane* 11, 505 (1900); see also: Róth and Richter, *Berl. klin. Wochenschr.* 1899, No. 30-31; Lindemann, *Deutsches Archiv f. klin. Med.* 65, Heft 1-2; Richter, *Berl. klin. Wochenschr.* 1900, No. 7; M. Senator, *Deutsche med. Wochenschr.* 1900, No. 3; Albarran, Bousquet, Bernard, IV. Session de l'association française d'urologie 1899; Claude et Balthazard, *Presse médicale* 1900, No. 14; Kümmel, 29. Kongress deutscher Chirurgen, Berlin 1900; Illyés, Sitzung der Budapester königl. Gesellschaft der Ärzte, 30. April, 1900; A. v. Korányi, discussion at the same; Moritz, *St. Petersburger med. Wochenschr.* 1900, No. 22; Kövesi and Róth-Schulz, *Berl. klin. Wochenschr.* 1900, No. 15; Claude and Balthazard, *La Cryoscopie des Urines*, Paris 1901.

By numerous experiments v. Korányi has proved that one sound kidney suffices to maintain the normal depression of the freezing-point of the blood (0.56); so that an increase to something above 0.57–0.58 indicates that both kidneys are functioning imperfectly. The determination of the freezing-point of the blood is, therefore, of great importance in the diagnosis of such cases. The publications just cited contain numerous applications that can be made of facts thus obtained, into a detailed discussion of which we cannot, however, enter here.

The work done by the secretory cells of the kidneys in secreting the urine, the osmotic pressure of which is much higher than that of the blood, can be calculated, as Dreser\* has shown, by utilising the laws of osmotic pressure.

Calculation shows that when the kidney secretes, for example, 200 c.c. of urine, the energy required amounts to thirty-seven kilogram-metres; that is, the energy required is equal to that expended in raising a weight of thirty-seven kilograms to a height of one metre. Very considerable energy is therefore required.

#### THE PERMEABILITY OF BLOOD-CORPUSCLES.

For many years physiologists have studied the question, In how far are the red blood-corpuscles permeable to various dissolved substances?

Hamburger,† Grijns,‡ C.Eijkman,§ Schöndorff,|| Hedin,¶

\* Arch. f. exp. Path. u. Pharmakol. 29, 303 (1892).

† Dubois-Reymonds Arch., Physiol. Abt. 1886, 476; *ibid.* 1887, 31; Zeitschr. f. Biologie 26, 414 (1890).

‡ Jaarverslag van het Laboratorium te Weltevreden 1894; also Pflügers Arch. 63, 86 (1896).

§ Pflügers Arch. 68, 58 (1897).

|| *Ibid.* 63, 192 (1896).

¶ *Ibid.* 68, 229 (1897); 70, 525 (1898).



Köppe,\* Stewart,† Oker-Blom,‡ and others have tried by various methods to get an answer to this important question.§

Hedin's method rests upon the following considerations: If a substance is dissolved in blood-plasma so that a certain volume of the plasma contains a known amount of the substance, then the freezing-point of the plasma is lowered to a definite degree. This depression of the freezing-point is in most cases the same as though an equal amount of the substance had been dissolved in water.||

If now an equal amount of this same substance is dissolved in blood, the mixture is centrifuged, and the depression of the freezing-point of the blood-plasma determined, there are three possibilities. When  $A_1$  is the depression of the freezing-point shown by the solution of the substance in the blood,  $A_2$  that shown by the solution in the plasma, then:

$$1. A_1 > A_2,$$

or

$$2. A_1 = A_2,$$

or

$$3. A_1 < A_2.$$

If we presuppose that the substances in the blood capable of influencing the freezing-point of the plasma do not wander from the plasma into the blood-corpuses, or from

\* Dubois-Reymonds Arch., Physiol. Abt. 1895, 154; *ibid.* 67, 189 (1897).

† Journal of Physiology 24, 211 (1899).

‡ Pflügers Arch. 81, 167 (1900).

§ See also van Rysselberghe, Bulletins de l'Académie royale de Belgique No. 3, 173 (1901). Cited from a reprint.

|| This is explained by the fact that the proteids dissolved in the plasma because of their great molecular weight bring about only an exceedingly slight (practically no) depression of the freezing-point when dissolved in pure water.

the corpuscles into the plasma, when the substance to be investigated is added to the blood; and, also, that the addition of the substance does not alter the volume of the blood-corpuscles or the amount of plasma, these three possibilities may be explained as follows:

1. The dissolved substance is taken up either not at all or to a less degree by the blood-corpuscles than by an equal volume of plasma.

2. The substance has distributed itself equally between equal volumes of blood and plasma.

3. The blood-corpuscles have taken up a larger amount of the substance than equal volumes of plasma.

Such freezing-point determinations have been made with the Beckmann apparatus, and it has been found that the red blood-corpuscles are impermeable or perhaps only slightly permeable to NaCl, KCl, KNO<sub>3</sub>, NaNO<sub>3</sub>, KBr, and K<sub>2</sub>SO<sub>4</sub>.

Ammonium sulphate and ammonium phosphate do not enter the blood-corpuscles when small amounts (0.05 mol per litre) are added to the blood. If larger amounts are added (for example, 0.1 mol per litre), a part of these salts enters the blood-corpuscles.

The blood-corpuscles are permeable to ammonium chloride, ammonium bromide, and ammonium nitrate.

These results agree with those obtained by Grijns by other means. Only in the case of ammonium sulphate do the results of Hedin and Grijns differ. While the former found that the blood-corpuscles are permeable to this salt, the latter found that they are impermeable.\*

\* See also Overton, Vierteljahrsschrift der naturforschenden Gesellschaft in Zürich 40 (1895) and Zeitschr. f. physik. Chem. 22, 189 (1897).

Oker-Blom studied the same question by the conductivity method. The passage of a dissolved substance into the blood-corpuses was demonstrated by measuring the electrical conductivity of the blood.

Preliminary experiments had shown that the conductivity of the blood is dependent upon the electrolytes dissolved in the serum. The blood-corpuses behave like non-conducting particles that are suspended in the serum. By narrowing the path along which the electric current passes they increase the resistance, but otherwise they take no part in conducting the current.\* The electrolytes contained in the blood-corpuses, or those which enter them from the serum, do not affect the conductivity of the blood.

If now we wish to investigate the behaviour of a substance dissolved in the blood toward the blood-corpuses, then, by determining the conductivity of this solution and comparing it with the conductivity which the solution would have if the dissolved substance had not entered the blood-corpuses, it can be ascertained whether the blood-corpuses are permeable or impermeable to the substance under investigation. If the former is the case, a certain amount of the dissolved substance will be withdrawn from the serum, and the conductivity of the blood will be correspondingly diminished.

The measurements of Oker-Blom lead to the same conclusions as those of Hedin.

The observations that have been made on

\* Oker-Blom, *Pflügers Arch.* 79, 111 and 510 (1900); E. Cohen, *Zeitschr. f. physik. Chem.* 28, 723 (1899).

## THE OSMOTIC PRESSURE BETWEEN MOTHER AND CHILD

are very instructive, especially in so far as they show the precautions that must be taken to obtain freezing-point determinations that are free from criticism.

These observations, first made by Veit,\* and more recently by Krönig and Fueth,† may be of great importance in the physiology of the metabolism between mother and child.

By determining the freezing-point of the blood of mother and foetus, Veit found that the osmotic pressure of the latter exceeds that of the former. As an average he found  $\Delta=0.579$  for the freezing-point of the foetal blood, and  $\Delta=0.551$  for that of the maternal blood.

Now we know (see p. 179) that a depression of the freezing-point of one-thousandth of a degree corresponds to an osmotic pressure of 0.012 atmosphere. The pressure excess of the foetal blood therefore amounts to  $(579-551) \times 0.012$  atmosphere = 0.336 atmosphere = 255 mm. of mercury, according to Veit's measurements.

Since it is hard to understand how so delicate a membrane as the chorion which separates mother and child is able to withstand such a pressure, Krönig and Fueth doubted the results obtained by Veit and repeated these measurements. In the experiments of Krönig and Fueth particular attention was paid to the technique of the freezing-point determinations.

When this was done it was found (as might have been expected!) that even very carefully prepared thermome-

\* Zeitschr. f. Geburtsh. u. Gynäkol. 42, 316 (1900).

† Monatsschr. f. Geburtsh. u. Gynäkol. 13, 1 (1901).

ters may show certain errors in graduation which, when their amount is not determined by specially prepared experiments, may seriously impair the accuracy of freezing-point determinations. "We have purposely pointed out this difference of about nine one-thousandths of a degree at  $-0.5^{\circ}$  between our two thermometers in order to show that errors in graduation within  $\frac{1}{100}$  of a degree may occur even in ideally working instruments of precision. This may explain many a difference in the freezing-point of the blood as determined by different observers. It is in the freezing-point determinations that have thus far been made by medical men that we generally miss any reference whatsoever to the average error made in obtaining the average result, and to errors in the graduation of the instrument."

If we scan the data obtained by Krönig and Fueth we find that the depression of the freezing-point of the foetal blood and of the maternal blood is the same; that (at the end of gestation) the blood of the mother is in osmotic equilibrium with that of the child.

In harmony with Veit, these authors found that the osmotic pressure of the amniotic fluid is lower than that of the maternal (or foetal) blood.

In conclusion I wish to point out again that the chemical analysis of animal fluids can give us no idea of their osmotic behaviour. Krüger \* and Scherenziss † have made gravimetric analyses of incinerated blood. In the incineration, however, many of the organic substances of the blood,

\* Untersuchungen über das fötale Blut im Momente der Geburt, Dissertation. Dorpat 1886.

† Ibid. Dorpat 1888.

which because of their high molecular weight contribute practically nothing at all to the osmotic pressure, are converted into salts. Even though the amount of these salts be determined, they tell us nothing concerning the substances (in the blood) from which they came originally.

## FIFTEENTH LECTURE.

### Applications (Continued).

#### OSMOTIC ANALYSIS.

THE freezing-point of a solution, and therefore that of any animal fluid (such as blood-serum or urine), is dependent upon the number of molecules dissolved in a definite volume of the same, bearing in mind that in case electrolytes are present the ions count as independent molecules (see p. 196).

If we wish to ascertain the number of mols present in one litre of such an (aqueous) fluid by determining its freezing-point, we determine, first of all, its specific gravity. If this is equal to  $S$ , then the weight of one litre of the fluid is  $1000S$  grams. If the weight of the substances in solution (that is, the sum of the electrolytes and the non-electrolytes) is  $p$  grams, then the weight of the water in  $1000S$  grams of the fluid is  $(1000S - p)$  grams.

We first determine the freezing-point of the liquid and find, for example,  $\Delta^\circ$ . If one mol were dissolved in 100 g. of water, the freezing-point of this solution (according to p. 174) would be depressed  $18.6^\circ$ . Since, however, the depression of the freezing-point is  $\Delta^\circ$ ,  $\frac{\Delta}{18.6}$  mols of dissolved substance are present in 100 g. of water, or in  $(1000S - p)$  grams of water  $\frac{1000S - p}{100} \cdot \frac{\Delta}{18.6}$  mols.

At Hamburger's suggestion\* we shall designate the number of mols (that is, the number of gram-molecules + gram ions, consequently all the particles that contribute to the osmotic pressure) contained in the litre, the *osmotic concentration* of the physiological fluid, and shall represent this by the symbol  $C_o$ . By definition:

$$C_o = \frac{1000S - p}{100} \cdot \frac{\Delta}{18.6}$$

If the fluid has only a low concentration, that is, if  $p$  has only a small value, then its specific gravity will not differ greatly from unity, and we may write the above equations thus:

$$C_o = \frac{1000}{100} \cdot \frac{\Delta}{18.6} = \frac{\Delta}{1.86}$$

We therefore find the *osmotic concentration* of the fluid by dividing its freezing-point by 1.86.

Now we can conceive of the *osmotic concentration* as the sum of the two other values; if we take blood-serum, for example, we see that each of the substances dissolved in it contributes to its osmotic pressure. These substances are non-electrolytes and electrolytes. If we designate the concentration of the non-electrolytes by  $C_{ne}$ , the concentration of the electrolytes by  $C_e$ , then

$$C_o = C_{ne} + C_e$$

The question now arises, How can each of the factors in this equation be determined in any given case?

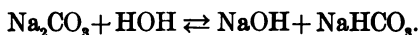
Bugarszky and Tangl † have answered this question for blood-serum; they have made an *osmotic analysis* of the same.

\* Personal communication.

† Pflügers Archiv 72, 51 (1898).



The most important electrolytes present in serum are the inorganic salts, NaCl and Na<sub>2</sub>CO<sub>3</sub>. The presence of hydroxyl ions in the blood, which give it its alkaline reaction, is probably to be attributed, in the main, to the hydrolytic splitting of the sodium carbonate contained in the serum. This splitting takes place according to the equation



For the observations of Shields \* have shown that sodium carbonate is hydrolytically dissociated in the manner given above to about 7 per cent in the concentration in which it is found in the blood.

The concentration of the organic salts (which are also electrolytes) compared to that of the inorganic is so slight that we may consider the electrical conductivity of the serum as a measure of the concentration of the inorganic molecules.

At all events, for reasons which have already been discussed (see pp. 278 and 279), the conductivity is a more accurate measure of the number of inorganic molecules in the serum than the amount of ash it yields.

If now, without anything further, we were to draw any conclusions concerning the concentration of the electrolytes in serum from its electrical conductivity, we should commit an error. For proteids are also dissolved in the serum, and these diminish the conductivity of the electrolytes. Experiments especially arranged for this purpose have shown that the addition of one gram of these proteids to the electrolytes which are contained in 100 c.c. of serum diminish the conductivity about 2.5 per cent.

\* Zeitschr. f. physik. Chem. 12, 167 (1893).

Taking this fact into consideration, when the conductivity ( $\chi_s$ ) of the pure serum has been measured and corrected as here described, the concentration of the electrolytes in the serum may then be determined as follows:

By titration the chlorine content of the serum is determined. Since the amount of sodium in the serum is much greater than the amount of sodium that is chemically equivalent to the chlorine determined in this way, the latter is counted as sodium chloride.

From the measurements of Kohlrausch, who has determined the conductivity of sodium chloride solutions of different concentrations, is calculated the conductivity ( $\chi_{\text{NaCl}}$ ) of the sodium chloride solution the concentration of which is equal to that of the serum. If this is subtracted from the conductivity found for the serum ( $\chi_s$ ), we get the conductivity ( $\chi_s - \chi_{\text{NaCl}}$ ) of the electrolytes that are present in the serum outside of the sodium chloride. The most important of these is the conductivity of the sodium carbonate ( $\chi_{\text{Na}_2\text{CO}_3}$ ).

We now calculate the concentration of a  $\text{Na}_2\text{CO}_3$  solution that has the conductivity ( $\chi_s - \chi_{\text{NaCl}}$ ), using the measurements of Kohlrausch as our basis.

Since in the determination of the osmotic concentration ( $C_o$ ) both the undissociated molecules  $\text{NaCl}$  and  $\text{Na}_2\text{CO}_3$ , and their ions take part in bringing about the observed depression of the freezing-point, we must ascertain the degree of dissociation of the sodium chloride and the sodium carbonate; for the number of molecules + ions present in a solution the freezing-point of which has been determined depends upon the degree of dissociation of these substances.

If  $a$  is the number of mols of  $\text{NaCl}$  in a definite volume

when no dissociation has occurred, and  $b$  the number of molecules (+ions) after this has taken place, then (see p. 199)

$$b = i \times a.$$

Now since

$$i = 1 + (k-1)\alpha,$$

$$b = \{1 + (k-1)\alpha\}a.$$

Now  $k$  equals 2 for NaCl, wherefore  $b_{\text{NaCl}} = a(1 + \alpha)$ .

For  $\text{Na}_2\text{CO}_3$ ,  $k$  equals 3, wherefore  $b_{\text{Na}_2\text{CO}_3} = a(1 + 2\alpha)$ .

The values of  $\alpha$  are calculated (see p. 209) from the electrical conductivities of the NaCl and the  $\text{Na}_2\text{CO}_3$  solutions.

In the manner described the following data were obtained for the serum of the horse:

1. NaCl content, 0.086 gram-equivalent per litre.
2. Degree of dissociation  $\alpha$  of a NaCl solution of this concentration,  $\alpha = 0.841$ .
3. There are therefore present as molecules+ions:

$$0.086\{1 + (2-1)0.841\} = 0.158 \text{ mol per litre.}$$

4.  $\chi_s$  at  $18^\circ = 0.0125$ .
5.  $\chi_{\text{NaCl}}$  according to Kohlrausch = 0.00796.
6.  $\chi_s - \chi_{\text{NaCl}} = 0.0125 - 0.00796 = 0.00458$ .
7. According to Kohlrausch this conductivity corresponds to that of a  $\text{Na}_2\text{CO}_3$  solution which contains 0.0298 mol per litre.
8. The degree of dissociation of this solution is 0.692.
9. There are therefore present as molecules+ions

$$0.0298\{1 + (3-1)0.692\} = 0.071 \text{ mol per litre.}$$

10. The concentration of the electrolytes of the serum consequently amounts to

$$C_s = 0.158 + 0.071 = 0.229 \text{ mol per litre.}$$

The osmotic concentration of the serum,  $C_o$ , is calculated from the equation (see p. 281)

$$C_o = \frac{\Delta}{1.86}.$$

The freezing-point was found to be 0.527, wherefore

$$C_o = \frac{0.527}{1.86} = \mathbf{0.283} \text{ mol per litre.}$$

Now since  $C_s = \mathbf{0.229}$  " " "

$$C_{na} = C_o - C_s = \mathbf{0.054} \text{ mol per litre.}$$

These non-electrolytes of the serum are the non-dissociated organic compounds dissolved therein. Only a very small proportion of the organic substances present are electrolytically dissociated. These are the organic salts which are present in only small amounts. We may therefore consider the concentration of 0.054 mol per litre as the concentration of the organic molecules.

In the above-described manner Bugarszky and Tangl obtained the following data:

Kind of serum.	Specific gravity at 18°.	Osmotic concentration, $C_o$ .	Concentration of the electrolytes, $C_e$ .	Concentration of the non-electrolytes, $C_{na}$ .
Horse .....	1.0277	0.302	0.233	0.069
Dog .....	1.0240	0.323	0.239	0.084
Ox .....	1.0266	0.330	0.242	0.088
Hog .....	1.0309	0.332	0.244	0.088
Sheep .....	1.0271	0.334	0.256	0.078
Cat.....	1.0273	0.342	0.264	0.078

We cannot discuss in detail many of the interesting conclusions that may be drawn from these data; yet two are to be especially emphasised:

1. The specific gravity is no index of the osmotic concentration of the serum.

This holds also for the urine. If we remember that the mean specific gravity of ox serum is 1.0266 (at 18°), while that of horse serum is 1.0277, and that in spite of this the former has a higher osmotic concentration (0.330 mol per litre) than the latter (0.302), the correctness of this conclusion becomes at once apparent.

2. The total ash is no correct measure of the osmotic concentration of the electrolytes present in the serum. We have already given the reasons for this above (cf. p. 278).

Only by combining chemical analysis with the described physico-chemical methods can we get an insight into the osmotic behaviour of animal fluids.

In considering the theory of disinfection (see p. 236), we discussed the

#### POISONOUS EFFECTS

of different chemical agents upon bacteria. We shall now consider such effects in a more general way.

The first systematic observations in this direction date from 1896, when Kahlenberg and True,\* and Heald,† studied the poisonous effects of dilute solutions of various acids, bases, and salts upon plants, and tried to explain their results in the light of the theory of electrolytic dissociation.

In these experiments the freshly germinated seeds of *Lupinus albus L.*, *Pisum sativum*, *Zea Mais* or *Cucurbita Pepo* were introduced into various solutions and the con-

\* Botanical Gazette 22, 81 (1896); see also True and Hunkle: Über die Wirkung der Phenole auf *Lupinus albus*, Botanisches Centralblatt 76, 289, 321, 361, 391 (1898).

† Ibid. 22, 125 (1896); see also Stevens, *ibid.* 26, 377 (1898) and Guéguen, Bulletin Soc. mycol. de France 15, 138 (1899).

centrations of the latter were determined at which the plants began to die or were just able to develop.

In this way it was found that the poisonous action of hydrochloric, hydrobromic, nitric, and sulphuric acids is the same. If one gram-equivalent is contained in 3200 litres of the solution, the plants die, while in solutions which contain one gram-equivalent in 6400 litres they remain alive.

Since in these very dilute solutions only the ions of the dissolved substance are present (that is to say, only hydrogen and chlorine ions, hydrogen and bromine ions, hydrogen and  $\text{NO}_3$  ions, hydrogen and  $\text{SO}_4$  ions), and since the anions ( $\text{Cl}$ ,  $\text{Br}$ ,  $\text{NO}_3$ ,  $\text{SO}_4$ ) are non-poisonous,—for the sodium salts of these acids are non-toxic at the same concentration (see p. 263),—both Kahlenberg and True, and Heald, concluded that the toxic effects observed are due to the hydrogen ions.

Even though this conclusion is, in the main, correct, Jacques Loeb \* has brought forward some important objections to the described experiments, on the ground that the limit of the toxic action was not determined accurately enough.

Were the objection to be raised that the action of these acids which are poisonous at a concentration of one gram-equivalent in 3200 litres, but non-poisonous at a concentration of one gram-equivalent in 6400 litres, is dependent, not upon the number of hydrogen ions but upon the per cent of acid in the unit volume of solution, this criticism could not be overcome by the data obtained by Kahlenberg and True or by Heald. To this is to be added the

\* Pfügers Archiv 69, 1 (1897).

fact that the time at which the growth of seedlings ceases cannot be accurately determined, especially when the experiments are allowed to run through the night.\*

Jacques Loeb † has also studied the physiological effects of the ions of different electrolytes. As an index of the toxicity of the solution of an electrolyte he chose the amount of water absorbed by the gastrocnemius muscle of the frog when immersed in it—a reaction that enabled him to determine accurately the effect of the electrolyte under investigation.

Loeb found that this muscle shows no variation in weight in a 0.12 normal sodium chloride solution (=0.7 per cent). If, however, a trace of an acid or an alkali is added to this solution, the weight of the muscle (in consequence of an absorption of water) is increased.

Now it was found that muscles immersed for one hour in a  $\frac{1}{10}$ N. sodium chloride solution containing one gram-equivalent of  $\text{HNO}_3$ ,  $\text{HCl}$ , or  $\text{H}_2\text{SO}_4$  per 210 litres, increase in weight as follows:

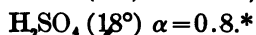
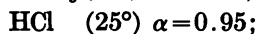
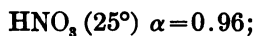
\* When the data obtained by Kahlenberg and True and by Heald are compared with those obtained previously by Nägeli (see p. 46) such considerable differences are found to exist that they can with difficulty be attributed to the greater sensitiveness of the material (cells of *spirogyra*) employed by the latter. A repetition of these experiments is therefore much to be desired. See also the observations in this direction of Ch. Richet, *Archives de Physiologie* 10, 145 and 366 (1882); Fischer, *Zeitschr. f. Hyg. und Infektionskr.* 25, 102 (1897); Coupin, *Compt. rend.* 130, 791, 864 (1900); Devaux, *ibid.* 132, 719 (1901); 133, 58 (1901).

† *Pflügers Arch.* 69, 1 (1897); 71, 457 (1898); see also Loeb, *Pflügers Arch.* 75, 303 (1899); *Festschrift f. Fick. Braunschweig*, 101 (1899); *Am. Jour. Physiol.* 3, 383 (1900); *ibid.* 3, 327 (1900); *ibid.* 5, 361 (1901); *ibid.* 6, 411 (1902); *Pflügers Arch.* 88, 68 (1901); *ibid.* 91, 248 (1902). For an English review of Loeb's work on the physiological effects of ions see M. H. Fischer, *Medical Record*, March 30, 1901; also Butler's *Materia Medica and Therapeutics*. Saunders & Co., 1902.

	I.	II.	III.	IV.	V.	Average.
HNO <sub>3</sub> .....	8.6%	7.6%	7.3%	7.6%	8 %	7.8%
HCl.....	8.2	7.8	7.6	7.6	7.6	7.7
H <sub>2</sub> SO <sub>4</sub> .....	8.4	6.7	7.9	7.9	9.6	8.1

This table shows that solutions of these acids containing the same number of gram-equivalents in the same volume have the same physiological effects.

If now we wish to discover in how far this action is to be attributed to the hydrogen ions, we must ascertain how many of the acid molecules are dissociated into their ions. The degree of dissociation of the acids at the concentration employed was ascertained by determining their electrical conductivity (see p. 200) whereby it was shown that for



In the case of nitric acid, therefore, 95 per cent of the nitric acid molecules are dissociated into their ions, while only 5 per cent of undissociated molecules are present in the solution. We may therefore conclude that the action of the nitric acid is, at the concentration employed, mainly an ion effect. Now considerations similar to those given on p. 263 lead to the conclusion that it is the hydrogen ions that bring about the described physiological effect—an absorption of water by the muscle.

Solutions of the acid salts KHSO<sub>4</sub> and NaHSO<sub>4</sub> have a similar effect upon the gastrocnemius muscle; the physiological action of these is also the same when the same number of hydrogen ions are present in the unit volume of solution.

\* This figure is uncertain.



A muscle immersed in a sodium chloride solution to which has been added a small amount of an alkali also shows an increase in weight. In this case it is the hydroxyl ions that bring about the absorption of water.

To explain this absorption of water by muscle when subjected to the action of hydrogen or hydroxyl ions, Loeb assumes that the hydrogen (or hydroxyl) ions which enter the muscle bring about a splitting of the proteids present in it. In consequence the large molecules give rise to a greater number of smaller ones, and the osmotic pressure of the fluids found in the muscle is increased. As a result the muscle absorbs water to a corresponding degree from the solution in which it lies, and this increases its weight.

In discussing the taste of dilute solutions we saw that the behaviour of acetic acid is different from that of the stronger acids, in that no relation exists between the sour taste of this acid and the concentration of its hydrogen ions (see p. 265).

It is a noteworthy fact that acetic, lactic, and malic acids also bring about a greater absorption of water by the gastrocnemius muscle than would be expected from the concentration of the hydrogen ions.

An explanation of these facts is still lacking.

In conclusion I wish to speak briefly of Maillard's \* investigations, since they, best of all, enable us to judge of the status of the entire question at this moment, and since

\* *Bulletin de la Soc. chimique de Paris* 21, 16 (1899); *Compt. rend. de la Soc. de Biologie*, 4 janvier 1899; *Journal de Physiologie et de Pathologie générale*, juillet 1899, cited from a reprint; see also: Guéguen, *Bulletin Soc. mycolog. de France* 14, 201 (1898); *ibid.* 15, 15 (1899); Trabut, *Bulletin Soc. botan. de France* 42, 33 (1895); J. F. Clark, *Jour. of Physical Chemistry* 5, 289 (1901).

they point the way that must be followed in order to attain our end.

According to Maillard, all the experiments thus far made err in that the osmotic phenomena which play a rôle in them have been ignored.

If we examine the following table taken from the experiments of Paul and Krönig (see p. 240) on the disinfectant action of sublimate solutions, we see that the very apparent effect of the addition of sodium chloride upon the toxic action of the bichloride in the first column is markedly reduced in the second:

DILUTION OF 16 LITRES.		DILUTION OF 256 LITRES.	
Time, 12 minutes.		Time, 30 minutes.	
HgCl <sub>2</sub> .....	0 colonies		10 colonies
HgCl <sub>2</sub> + 2NaCl....	3 “		13 “
HgCl <sub>2</sub> + 10NaCl..	469 “		16 “

Now in the second series of experiments the concentration of the corrosive sublimate is not only lower than that in the first series, but the time during which the solutions have acted is also much greater. It is therefore possible that the toxic effect of the bichloride is a function not only of its concentration, but also of the time that it is allowed to act.

If the latter is not sufficiently long, the sublimate molecules (or mercury ions) cannot diffuse into the interior of the animal (or vegetable) organism, and consequently cannot exert their toxic effects. We can judge of these effects only when the substances examined are given sufficient time to enter the organism by diffusion, and when the toxic action is not measured until osmotic equilibrium is established.

Paul surmised that the velocity of diffusion plays a rôle

in the disinfectant action of different chemical agents, for at his suggestion Eckhardt\* investigated the diffusion velocity of different disinfectants. In these investigations it was found that a parallelism exists between this velocity and the germicidal effect of disinfectants upon certain bacteria.†

Maillard's observations are based upon these considerations, and aim to determine the toxicity of copper sulphate for *Penicillium glaucum*.

Cultures of this mould were put into glass flasks, and kept at 18° in a thermostat (variations in temperature about 1 per cent).

Copper sulphate solutions of various concentrations to which had been added the substances necessary for the nourishment of the mould were then introduced into the flasks. The moulds were permitted to develop for about five weeks, during which time osmotic equilibrium was established between the liquids within and without the cell.

The flakes of mould which developed in the solutions were then filtered off, dried, and weighed. The following table shows how the weight of the cultures is dependent upon the concentration of the copper ions in the solutions.

Number of gram ions of copper.	Weight of the cultures.
0.0803	0.0166
0.0647	0.0442
0.0554	0.0505
0.0329	0.0649

\* Über die Diffusion und ihre Beziehung zur Giftwirkung: Inaugural Dissertation, Leipzig 1898.

† In the investigations of Kahlenberg and Austin on the action of sodium salts upon *Lupinus albus* [Journal of Physical Chemistry 4, 553 (1900)], and those of Kahlenberg and Mehl [ibid. 5, 113 (1901)], the rôle of diffusion is not taken into consideration.

The weight of the cultures decreases as the number of copper ions in the unit volume increases; in other words, the toxic effect of a solution increases as the concentration of the copper ions increases.

If in a certain solution the dissociation of the copper sulphate is decreased by the addition of a salt containing a common ion (for example,  $(\text{NH}_4)_2\text{SO}_4$  or  $\text{Na}_2\text{SO}_4$ ), the toxicity of the copper sulphate solution is diminished—a proof of the correctness of the assumption that the toxic effect of this solution is attributable to the presence of free copper ions.

How very complicated the question is, and how little we can say at present that the theory of electrolytic dissociation suffices to explain it, is perhaps best shown by the interesting observation of J. F. Clark\* that the toxic action of many acids (upon many vegetable organisms) is *diminished* when their dissociation is increased.

\* Journal of Physical Chemistry 3, 263 (1899); Botan. Gazette 28, 289, 378 (1899), where references to the literature may be found. See also True, *ibid.* 26, 407 (1898); American Journal of Science (4) 9, 183 (1900).

## SIXTEENTH LECTURE.

### Electromotive Force.

If a copper rod is dipped into a copper sulphate solution contained in a porous cup, and this is placed in a zinc sulphate solution into which is dipped a zinc rod, the entire system constitutes, as you know, a galvanic element (Daniell cell).

If the zinc is connected with the copper by a wire, an electric current flows through it. The existence of this current can be proved by letting it act in an appropriate manner upon a magnetic needle, which in consequence is deflected.

It may also be known to you from your knowledge of physics that the development of the electric current is attributed to the so-called *electromotive force* of the element.

The question as to how this force comes into existence even Volta\* attempted to answer. Volta believed that the electromotive force was located at the point of contact of the two metals (in the Daniell cell, therefore, where the copper and zinc are in contact with each other). Upon the other hand, some believed that the contact of the two liquids (in the Daniell cell the copper sulphate and zinc sulphate solutions) is the cause of the electromotive force, while others thought that its origin must be attributed to

\* See, among others, Ostwald, *Geschichte der Electrochemie*, Leipzig 1896.

the contact between the metals and the solutions of the electrolytes contained in the cell.

We are indebted to Nernst \* for the theory of the galvanic element which is based upon the theories of osmotic pressure and electrolytic dissociation, and which explains not only qualitatively but also quantitatively the phenomena observed in galvanic cells.

Before we direct our attention to this theory, however, we shall discuss in some detail the system of measurements which is at present generally employed in electrical work. Considering the extensive use made of electricity in daily life, a more accurate knowledge of this system is greatly to be desired.†

As is known to you, the resistance ( $R$ ) of a conductor is defined as the relation between the electromotive force (*tension, difference in potential*) ( $E$ ) and the amount of electricity which is driven through the conductor in the unit of time in consequence of this tension (*strength of current*). If the latter is represented by  $i$ , then

$$R = \frac{E}{i}, \quad (1)$$

or

$$E = iR. \quad (2)$$

This equation represents the well-known *Ohm's Law*. As the unit of resistance has been chosen the resistance of a mercury column at 0°, 106.3 cm. long and 1 sq. mm. in diameter. This unit of resistance is called one *ohm* ( $\Omega$ ). The unit of electromotive force has been chosen of such a magnitude, that the Weston normal element, with which we shall become acquainted immediately, has an electro-

\* Zeitschr. f. physik. Chem. 4, 129 (1889).

† See also F. Kohlrausch, *Die Energie oder Arbeit*, Leipzig 1900.

motive force of 1.0187 units at 15°. This unit of electromotive force is called one *volt*.

From equation (1),

$$i = \frac{E}{R}.$$

If herein

$$E=1 \quad \text{and} \quad R=1,$$

then  $i=1$ . The unit of the amount of electricity is the amount which in the unit of time (1 second) flows through a conductor the resistance of which is one ohm, and between the ends of which exists a difference of potential of one volt. The unit of the amount of electricity is called a *coulomb*, and the unit of current strength corresponding to this amount, one *ampère*.

If, therefore, 0.5 coulomb of electricity flows through a conductor per second, the current strength in this conductor amounts to 0.5 ampère.

It has already been pointed out (see p. 209) that Faraday's \* observations showed that the movement of electricity in electrolytes is always accompanied by a simultaneous movement of ions.

Furthermore, it was found that chemically equivalent amounts of different ions migrate with equal amounts of electricity (Law of Faraday). The meaning of this law is as follows:

If a certain amount of electricity, for example one coulomb, is sent through solutions of different electrolytes, such as copper sulphate and silver nitrate, the amounts of copper and silver that migrate with this amount of electricity (1 coulomb) are to each other as the chemically

\* See Ostwald, *Klassiker der exakten Wissenschaften*, No. 81, 86, 87.

equivalent weight  $\left( = \frac{\text{atomic weight}}{\text{valence}} \right)$  of the copper is to that of the silver—that is, therefore, as  $\frac{63.6}{2} : \frac{107.93}{1}$ .

If electrolysis occurs, that is, if the ions carried by the current through the electrolyte give up their electrical charges to the electrodes, whereby the copper or silver ions go over into the metallic (neutral) state, the amounts of the metals deposited upon the electrodes will also be to each other as their equivalent weights.

Now experiment has shown that when one coulomb per second of electricity flows through the solution of any silver salt—that is, when the current strength in such a solution is one ampère—1.118 mg. of metallic silver are deposited in one second from the solution upon the electrodes. This figure is called the *electrochemical equivalent* of silver.

The *electrochemical equivalent* of an ion is therefore the number of milligrams of this ion that are precipitated per second from one of its solutions by a current of one ampère.

If one gram-equivalent, 107.93 grams, of silver is to be precipitated from any silver solution,  $\frac{107.93}{0.00118} = 96538$

coulombs must be sent through this solution. It may therefore be said that the electrical charge of one gram-ion of silver is 96538 coulombs.

Now according to Faraday's law the same amount of electricity is united with equivalent amounts of different ions (silver, copper, iron, etc.). A gram-equivalent of any ion is therefore charged with 96538 coulombs; and conversely, in the movement of 96538 coulombs through a solution one gram-equivalent migrates, or is precipitated, when the conditions necessary for the latter are at hand.



These facts make it possible to measure the strength of an electric current by a *voltameter (coulometer)*\*—an apparatus in which an electrolyte is decomposed by an electric current the strength of which is to be determined.

In its simplest form such a voltameter consists of a beaker containing a copper sulphate solution. Into this dip two copper plates which are connected with the electric current of which we wish to determine the strength.

If the amount of copper deposited after a certain time upon the negative electrode is determined by weighing, the strength of the current can be calculated from the law of Faraday.

If, for example, a certain current deposited 5 g. of copper in 5 minutes, what would be the strength of the current?

We know that in case the current strength were one ampère, 1.118 mg. of silver would be precipitated from a silver solution per second. With the same current an amount of copper would be precipitated from the copper sulphate solution which would be to the amount of silver precipitated from the silver solution as the equivalent weight of the copper ( $\frac{63.6}{2}$ ) is to that of the silver ( $\frac{107.93}{1}$ ). If  $X$  is the number of milligrams of copper precipitated per second from the copper solution with a current strength of 1 ampère, the following equation holds:

$$X : 1.118 = \frac{63.6}{2} : \frac{107.93}{1},$$

$$X = 0.3294 \text{ (mg. copper per second).}$$

In five minutes ( $= 5 \times 60 = 300$  seconds) a current of 1 ampère would precipitate  $300 \times 0.3294$  mg. copper = 0.09882 g. copper.

Now since our current precipitates 5 g. copper during this time, its strength is

$$\frac{5}{0.09882} \text{ ampère} = 50.5 \text{ ampère.}$$

\* See Richards and Heimrod. Proceedings Amer Acad. of Arts and Sciences 37, No. 16, Feb. 1902.

The *electrical energy (electrical work)* that a battery or a dynamo can furnish may be compared with the energy furnished by a mass of water falling from a certain height. Just as the mechanical energy of the water is equal to the product of the amount of the falling water and the driving force, as determined by the height of the fall, so the electrical energy of a galvanic element (or dynamo) is equal to the product of the amount of electricity flowing through the wire and the electromotive force.

The unit of electrical energy (*joule*) may therefore be represented by the product: Unit of difference in potential  $\times$  unit of the amount of electricity—that is, volt  $\times$  coulomb. The electrical energy furnished per second may then be represented by the product: volt  $\times$  ampère. This unit is termed a *watt*. Considering the many technical applications made of electricity, it may be pointed out that 736 watts equal one *horse-power*—that is, are equal to the work done when 75 kg. are raised 1 m. per second. The following table contains a summary of the different relations that exist in the equation

$$1 \text{ ampère} = \frac{1 \text{ volt}}{1 \text{ ohm}}.$$

The strength of the current in ampères gives the number of coulombs that flow through a conductor per second.

1 volt  $\times$  1 coulomb = 1 joule (unit of electrical energy).

1 volt  $\times$  1 coulomb = 0.2362 calories.\*

1 volt  $\times$  1 ampère = 1 watt (work done per second).

736 watts = 75 kilogram-metres per second = 1 horse-power.

\* The measurements of Jahn, *Zeitschr. f. physik. Chem.* 20, 386 (1898), have shown that 1 volt-coulomb (= 1 joule) is equal to 0.2362 calorie—that is, the electrical energy of 1 joule is able to heat 0.2362 g. water from 0° to 1°.

## THE MEASUREMENT OF ELECTROMOTIVE FORCE.

Of the great number of different methods that may be employed to measure electromotive force (E.M.F.),\* we shall here describe only one, the so-called *compensation method* of Poggendorff, since this enables us to make very accurate measurements in a convenient way.

The principle underlying this method is the comparison of the electromotive force to be measured with one of known magnitude.

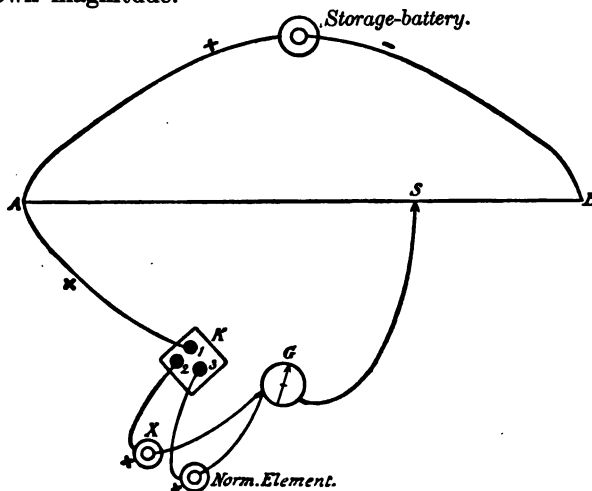


FIG. 41.

In Fig. 41 is given a diagram of the apparatus. Before we discuss this more fully, however, let us study the instruments employed in the measurements.

## THE NORMAL ELEMENTS.

Normal elements are elements, composed of metals and electrolytes, which experience has shown to be constant,

\* See G. Wiedemann, *Die Lehre von der Elektrizität*, 2. Aufl., 1893 to 1898, Braunschweig 1, 672; W. Clark Fisher, *The Potentiometer and its Adjuncts*. London, *The Electrician Series*.

readily constructed, and to have the same electromotive force under the same external conditions (temperature).\*

Two such elements are in use to-day, the cadmium normal element of Weston, and the zinc normal element of Latimer Clark; because of its excellent qualities the former will probably ultimately crowd out the latter.

Fig. 42 represents the Weston normal element.  $aAc$  is a two-armed glass vessel to which have been fused the glass capillaries  $F_1H_1$  and  $F_2H_2$ . Into  $c$  is introduced chemically pure mercury, into  $a$  a cadmium amalgam containing 12.8 per cent by weight of cadmium. This amalgam while still fluid is poured into the arm  $a$ , after a platinum wire which projects for a distance of one centimetre into the arm has been inserted into the capillary  $F_1H_1$ .

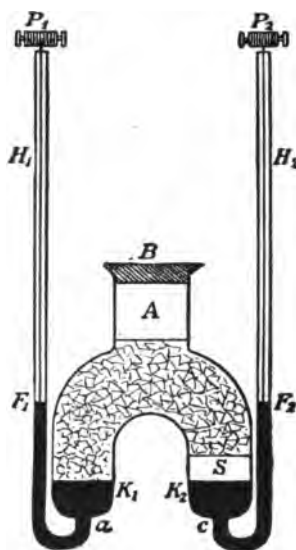


FIG. 42.

In a similar way a platinum wire is inserted through the capillary  $F_2H_2$  into the mercury contained in  $c$ .

Upon the mercury in  $c$  is put a paste  $S$ , consisting of a finely pulverised mixture of cadmium sulphate ( $\text{CdSO}_4 \cdot \frac{3}{2}\text{H}_2\text{O}$ ), mercury sulphate ( $\text{Hg}_2\text{SO}_4$ ), and metallic mercury. Part  $A$  of the cell is filled with moist, finely

\* For a collection of the literature see, among others, W. Jaeger, *Centralblatt für Akkumulatoren- und Elementenkunde* 1900 No. 1; 1901 No. 1-2. *Die Normalelemente*, Halle 1902.

powdered crystals of cadmium sulphate, upon which is poured a saturated (at about 30°) solution of cadmium sulphate.

The cell is closed with a rubber stopper covered with marine glue, care being taken that some air remains in the cell in *A* to prevent its breaking when heated.\*

If the element is heated to a certain temperature,  $t^\circ$ , it assumes the E.M.F. corresponding to this temperature after about one and a half hours. By an extensive series of measurements made in the course of several years by Jäger and Wachsmuth, in the Physikalisch-Technische Reichsanstalt of Charlottenburg, we have become very accurately acquainted with the E.M.F. of this cell at different temperatures, so that it has been possible to form an interpolation formula by means of which it is possible to calculate the E.M.F. of this cell for any temperatures between +10° and +26°.

This formula is the following:

$$E_t = 1.0186 - 0.000038(t - 20) - 0.00000065(t - 20)^2 \text{ volt.}$$

If, for example, we wish to know the E.M.F. of the Weston cell at 25°, we make  $t = 25$ , wherefore

$$\begin{aligned} E_{25^\circ} &= 1.0186 - 5 \times 0.000038 - 25 \times 0.00000065 \text{ volt} \\ &= 1.0184 \text{ volt.} \end{aligned}$$

In a similar way we find for 15°:

$$\begin{aligned} E_{15^\circ} &= 1.0186 + 5 \times 0.000038 - 25 \times 0.00000065 \text{ volt} \\ &= 1.0187 \text{ volt.} \end{aligned}$$

\* Explicit directions for making such cells can be found in Kahle, *Zeitschr. f. Instrumentenkunde* 13, 191 (1893), *Wiedemanns Ann.* 51, 203 (1894); Jäger and Wachsmuth, *Electrotechnische Zeitschr.* 15, 507 (1894); *Wiedemanns Ann.* 59, 575 (1896).

A difference in temperature of  $10^\circ$  consequently causes a change in the E.M.F. of only 0.0003 volt, or 0.03 per cent. This shows that if we are not dealing with determinations in which the greatest accuracy is necessary, we may neglect the temperature of the element altogether. It can therefore be employed at room temperature without the necessity of using a special thermostat.

The Clark element, which is still much used in physiology, is entirely similar in construction to the Weston element.

Into *a* (Fig. 42) is introduced a zinc amalgam, containing 10 per cent by weight of zinc, into *c* chemically pure mercury covered by a paste (*S*) made of a mixture of zinc sulphate crystals ( $\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$ ), mercury sulphate ( $\text{Hg}_2\text{SO}_4$ ), and metallic mercury.

*A* is filled with finely powdered crystals of zinc sulphate and a saturated (at  $30^\circ$ ) solution of the same. The element is closed and mounted in a way similar to that of the Weston element.

The interpolation formula which between  $0^\circ$  and  $30^\circ$  represents the E.M.F. of the Clark element is the following:

$$E_t = 1.4328 - 0.00119(t - 15) - 0.000007(t - 15)^2 \text{ volt.}$$

A simple calculation (see p. 302) shows that the E.M.F. of the Clark element varies about 0.0126 volt, that is, about 1 per cent, with a change in temperature of  $10^\circ$ . To prevent the errors that might arise from variations in temperature of several degrees, the cell must therefore be kept in a thermostat. It is, moreover, inconvenient that the Clark element requires a much longer time than the Weston element before it assumes the E.M.F. corresponding to the temperature at which it is used. These two disadvantages which the Clark element has when compared with the

Weston element are the reasons why the latter is at present superior to the former.\*

Fig. 43 represents a Clark (or Weston) element of a form frequently found upon the market. The cell is enclosed in a

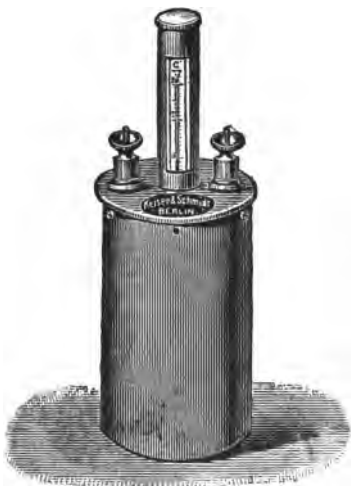


FIG. 43

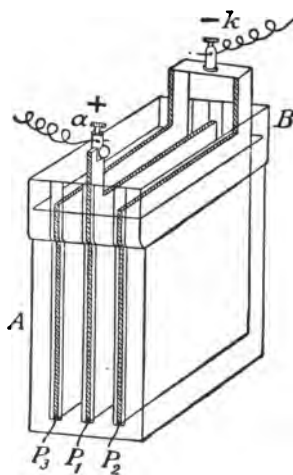


FIG. 44.

metal case, and carries in addition a sensitive thermometer.†

For reasons into the discussion of which we cannot enter here, the Weston element must not be used above 70° or below 10°, the Clark element not above 39°.

\* Concerning the elements manufactured by the European Weston Electrical Instrument Company see Jäger, l. c.

† Thermometers are given only with the Clark elements; for the Weston elements this would be superfluous. See the above.

## STORAGE CELLS.

Since these so-called secondary elements are much used by the physician, I wish to say a few words concerning their properties and their management.\*

Fig. 44 represents a storage cell.  $AB$  is a glass (or ebonite) trough filled with dilute sulphuric acid (136 volumes of concentrated chemically pure sulphuric acid, 1000 volumes of water).† The electrodes consist of the lead plates  $P_1, P_2, P_3$ .  $P_2$  and  $P_3$  are connected with each other;  $P_1$  is insulated from the two other plates by glass rods set between them.

If the plates are dipped into the dilute sulphuric acid, they gradually become covered with a thin layer of lead sulphate ( $PbSO_4$ ). If the storage cell is to be *charged*, that is, if we wish to introduce the electricity that is to be stored in it, we connect the binding-post  $k$  with the negative pole, the binding-post  $a$  with the positive pole of a dynamo, and let the current which the latter furnishes flow through the apparatus. After some time  $P_1$  becomes covered with a brownish-black layer of lead dioxide ( $PbO_2$ ), while  $P_2$  and  $P_3$  become covered with a layer of dull grey, spongy lead. We continue to charge the storage cell until there is a marked evolution of gas.

The chemical change that occurs in the process of charging the cell may be represented by the following equation:



\* For the practice of storage cells see, among others, K. Elbs, *Die Akkumulatoren*. 3. Aufl. Leipzig 1901. The theory of storage cells is extensively treated by F. Dolezalek, *Die Theorie des Bleiakкумуляtors*. Halle 1901.

† Great importance is to be attached to the purity of the sulphuric acid; traces of gold, platinum, or copper compounds are very harmful to the storage cell.

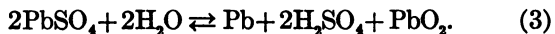


Immediately after charging, the electromotive force of the cell is about 2.6 volts. The electrical potential, however, soon falls, for reasons that we cannot discuss here, to 2 volts, if the storage cell is left to itself; after which it remains almost constant if the apparatus is kept on an open circuit (that is, giving no current).

If the storage cell is discharged by closing the circuit, the following chemical change takes place:



If entirely discharged, that is, if all the electricity which was previously stored in the storage cell is again taken away, the cell is in the same condition as before charging. Charging and discharging a storage cell are therefore reversible processes, and the two equations (1) and (2) may consequently be thus expressed:



It is to be noted that the strength of the charging and discharging currents is given by the manufacturers for every storage battery, and great importance is attached to the observance of these instructions, for, if neglected, the storage cell will be spoiled.

If the apparatus is discharged as directed, the electrical potential (2 volts) falls very slowly. When this has fallen to 1.8 volts, the cell should be recharged.

The electrical potential of the storage cell (2 volts) is connected with the chemical processes that go on in it. It is therefore independent of the dimensions of the apparatus, and we may make the general statement that every storage cell\* when fully charged has an electromotive force of 2 volts.

\* We are considering only lead-plate storage cells.

The amount of electricity that can be stored in a storage cell is dependent upon the amount of the so-called *active mass* present in the battery. This is the name given the lead dioxide which covers the positive electrode (or the spongy lead that covers the negative electrode). This amount of electricity is expressed in *ampère-hours*—that is, the number of hours that a current of one ampère can be obtained from the given storage cell before it is exhausted. This number of ampère-hours is called the *capacity* of the storage cell. A storage cell having a capacity of 50 ampère-hours is therefore one that furnishes a current of 1 ampère for 50 hours, or, what amounts to the same thing, a current of  $\frac{1}{2}$  ampère for 100 hours.

Conversely, to charge such a storage cell it will require a current of 1 ampère for 50 hours, or one of  $\frac{1}{2}$  ampère for 100 hours.\*

Strictly speaking, we do not obtain all the ampère-hours that it required originally to charge the storage cell when we discharge it, but, at the best, only 90 to 96 per cent of this amount (available effect in ampère-hours).

If, therefore, the available effect of a certain storage cell is 90 per cent, it means that of every 100 ampère-hours used in charging, 90 ampère-hours will be obtained upon discharging the storage cell.

The available effect in electrical energy (expressed in watt-hours) is usually less than 90 per cent, and, for reasons that cannot be discussed in detail here, amounts to about 85 per cent.

The internal resistance of a storage cell is very low, depending, of course, upon the dimensions of the apparatus,

\* Most storage cells require 5–10 hours to charge them, 4–8 hours to discharge them.

and usually amounts to only a few hundredths of an ohm. While charging the cell its resistance decreases; while discharging it the resistance increases.

It must be remembered that every storage cell in the course of time discharges itself; this occurs very slowly, however, so that good storage cells may be used without recharging even months after being charged. Yet it has been found best to recharge every cell that has not been used for some time before again putting it into regular service.

By *short-circuiting*, as it is called, that is, by discharging a storage cell by a stronger current than should be used according to instructions, the plates are bent, and the active mass is separated from them, whereby the storage cell is totally destroyed. Short-circuiting is therefore always to be avoided most carefully, and the cell is never to be discharged except through an ammeter, by which the strength of the discharging current can be controlled.

#### THE CAPILLARY ELECTROMETER AND THE GALVANOMETER.

In the measurement of electromotive force by Poggen-dorff's method, the one or the other of these instruments is used to show that no current is flowing through the circuit *GS* of the diagram in Fig. 41.

At present the capillary electrometer of Lippmann, of a form suggested by Ostwald,\* is much used.

Fig. 45 represents an electrometer of this form (about two thirds natural size), which, though not the most sensitive, has shown itself to be very convenient in general practice. The so-called Lippmann phenomenon, upon

\* See the description of the different forms in *Physico-Chemical Measurements*. Ostwald-Walker. Macmillan & Co., Ltd.

which the action of this instrument is based, is the following: If an electrolyte, for example dilute sulphuric acid, is poured upon mercury, and the difference of potential between the electrolyte and the mercury is altered at the surface of contact, the surface tension of the mercury is changed.

The capillary electrometer consists of two masses of mercury,  $k$  and  $k$ , separated by dilute sulphuric acid (1

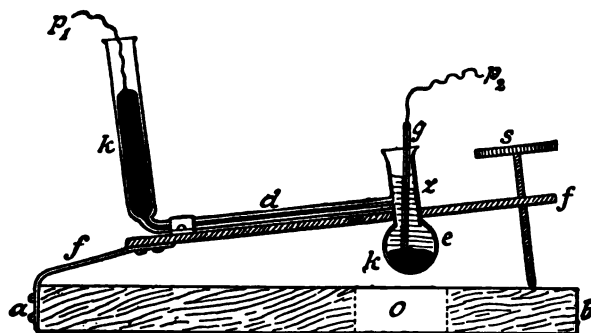


FIG. 45.

volume of acid, 6 volumes of water). The area of contact between the one mass of mercury and the electrolyte is large (at  $e$ ), the other small (in the capillary tube at  $d$ ). If the mercury column in the capillary tube at  $d$  assumes a certain state of equilibrium because of its surface tension, this will change when an electromotive force is introduced; in other words, the mercury will show a displacement in the capillary which will be a measure of the electromotive force introduced. Within narrow limits (about 0.1 volt), the movements of the mercury column may be considered proportional to the differences in potential between the two masses of mercury.

The capillary tube has a diameter of about 0.5 mm., and lies upon a scale which enables one to measure (by means of a microscope) the movements that occur in the mercury column.

Mercury is introduced into *k* and *e*, after which the dilute sulphuric acid is also introduced into *e*. The platinum wire *p*<sub>2</sub>, which is connected with the positive pole of the current, is covered with glass in order to insulate it from the sulphuric acid in *ge*. The end of *p*<sub>2</sub> dips into the mercury.

The position of the capillary tube can be altered by means of the screw *S*; the more perpendicular the position of the tube the less sensitive is the instrument, but the more rapidly does the mercury column come to rest.

The instrument can be made so that a difference in potential of 0.01 volt causes a movement in the column of mercury of about five divisions on the scale. If one fifth of the distance between two divisions on the scale be estimated, then the presence of a difference of potential of  $\frac{0.01}{25} = 0.0004$  volt can still be detected with such an instrument.

The apparatus should always be kept in short circuit, that is, *p*<sub>1</sub> and *p*<sub>2</sub> should always be connected with each other, except at the moment during which a measurement is made.

For this purpose the key illustrated in Fig. 46 is used. *p*<sub>1</sub> is connected with *c*, and *p*<sub>2</sub> with *b*. The binding-post *a* is connected with the general circuit.

If a galvanometer is used to detect a current, any sensitive instrument, such as the mirror galvanometer of Wiedemann, Thomson, or d'Arsonval, may be employed.

## THE PURIFICATION OF MERCURY.

Since in preparing normal elements and in filling capillary electrometers the use of chemically pure mercury is a

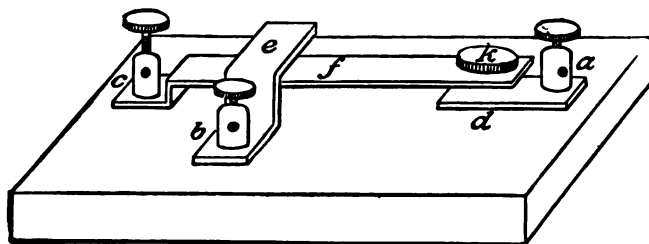


FIG. 46.

*conditio sine qua non*, I shall here describe how this is prepared according to the simple method of Hulett.\*

The mercury is first shaken up with a solution of mercurous nitrate in dilute nitric acid, in order to remove the major portion of the metals present in it as impurities. The mercury is then washed with water and dried by heating in a porcelain dish.

It is next introduced into the distilling apparatus illustrated in Fig. 47. *A* and *E* are two glass fractional distillation-flasks. *A* is set into an iron pot the bottom of which is covered with a thin layer of sand. *S* is a cylinder of asbestos board that gives passage to the side tube *D* and the neck of the flask *A*. The pot *P* is set upon a tripod and heated by a Bunsen burner. The neck of the flask *A* is narrowed at its upper end. Through this constriction passes the glass tube *fff* which is drawn out into a capillary at its lower end. The glass tube is held fast in the flask by a rubber tube that is pushed over the constricted portion

\* Zeitschr. f. physik. Chem. 33, 611 (1900).

of the neck of the flask. *B* is a thick-walled rubber tube that can be closed by the screw pinch-cock *C*.

The tube *D* (about 1½ m. long) passes into the fractional distillation-flask *E* through the rubber stopper *K*. Flask

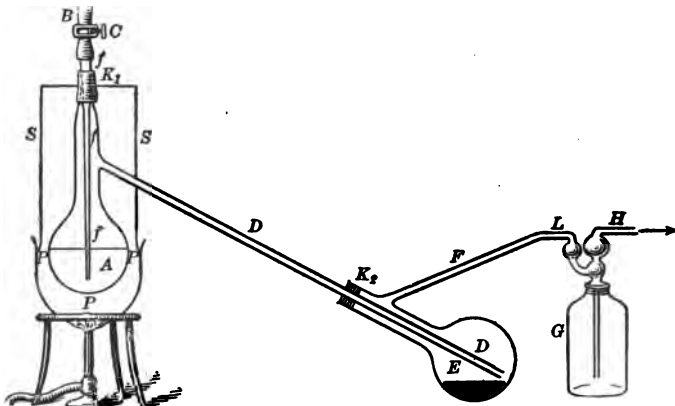


FIG. 47.

*E* communicates with the bottle *G*, which is connected with an hydraulic air-pump, and which serves to receive any water that may strike back from the water-pipe.

The mercury to be distilled is heated in *A*. If the hydraulic air-pump is set in operation and the stop-cock *C* is regulated so that a slow stream of air passes through *fff* into the mercury, distillation takes place without any "bumping." Depending upon the state of rarefaction of the air obtained in *A*, the mercury will distil over and collect in the flask *E* at from 180–200° C.

When distillation is at an end the fine dust of the metallic oxide which may have passed over into *E* with the mercury vapour is separated from the mercury by filtering it through filter-paper into which a number of fine holes have been punched with a needle. Mercury prepared in this way is pure enough to be used in electrical measurements.

We shall now consider how

THE MEASUREMENTS

are made with the described apparatus when set up as shown in Fig. 41.

If, for example, we wish to determine the electromotive force ( $X$ ) of a certain element, the circuit of the storage cell \* is closed through a great resistance  $AB$ , for example 10000 ohms.

$A$  is connected by wire with the paraffin (or ebonite) block  $K$ , which contains three mercury cups, 1, 2, 3; the wire dips into 1.

From the second cup a wire passes through the element to be measured,  $X$ , to the galvanometer  $G$ , and this is connected with the wire  $GS$ , which at  $S$  connects with a slider that can be moved along the wire  $AB$ .

From mercury cup 3 a wire passes to the normal (Weston) element, and this is, like  $X$ , connected with the galvanometer.

Care is to be taken that similar poles of the storage cell, normal element, and the element  $X$  are connected with the point  $A$ .

If now the cups 1 and 2 are connected by a bent wire, a point can be found by sliding  $S$  along  $AB$  where the galvanometer shows no deflection. If the electromotive force of the storage cell is  $E_A$ , that of the element  $X$ ,  $E_X$ , the following relation then exists: †

$$AS : AB = E_X : E_A,$$

\* Or storage cells; for the electromotive force in this portion of the circuit must always be greater than the electromotive force to be measured. Depending upon the magnitude of the latter, one or more storage cells are used.

† See, for example, G. Wiedemann, l. c. 1, 681.



or

$$E_x = E_A \frac{AS}{AB}. \quad (1)$$

Now if the electromotive force ( $E_A$ ) of the storage cell were absolutely constant,  $E_x$  would be known, for we know the value of  $AS$  and  $AB$ . Since the electromotive force of a storage cell is, however, subject to slight variations, we compare it, after completing the measurement just described, with the electromotive force ( $E_N$ ) of the normal element: we gauge the storage cell by the normal element.

To make this comparison we break the connection between the mercury cups 1 and 2 in Fig. 41, and connect 1 and 3. We then again determine the position of the slider upon the wire  $AB$  where the galvanometer is no longer deflected. If the slider stands at a point  $S_1$  upon  $AB$ , then the following holds:

$$AS_1 : AB = E_N : E_A,$$

or

$$E_A = \frac{AB}{AS_1} E_N. \quad (2)$$

We therefore now know the electromotive force of the storage cell ( $E_A$ ) expressed in that of the normal element ( $E_N$ ). If we write the value of  $E_A$  of equation (2) into equation (1), we find

$$E_x = \frac{AB}{AS_1} E_N \frac{AS}{AB},$$

or

$$E_x = \frac{AS}{AS_1} E_N.$$

Now since  $AS$ ,  $AS_1$ , and  $E_N$  are known, we know the value of  $E_x$  also.

Since a straight wire  $AB$  having a resistance of 10000

ohms would have to be inconveniently long, two rheostats (I and II) are used instead, which are connected in series and each of which has a resistance of 10000 ohms. All the plugs are inserted into the first rheostat; that is to say, no resistance is introduced; by withdrawing all the plugs from the second rheostat, 10000 ohms are introduced into the circuit.

If now a certain resistance is introduced into the circuit by removing a plug in I, a corresponding plug is put into position in II, whereby the resistance is decreased to a corresponding degree. In this way the sum of the resistances ( $AB$  in Fig. 41) remains constant (10000 ohms), while that in I (which corresponds to the end of the wire  $AS$  in Fig. 41) is changed in any desired way. This is the same as moving the slider  $S$  along the wire  $AB$ .

Suppose we wished to determine the electromotive force of a Daniell cell.

A resistance of 5452.8 ohms ( $= AS$ ) is introduced into the resistance-box I.

A resistance of 4547.2 ohms ( $= SB$ ) is introduced into the resistance-box II.

The galvanometer then indicates no current, wherefore

$$E_{\text{Daniell}} = \frac{5452.8}{10000} E_A.$$

To gauge the storage cell (determine  $E_A$ ), it is compared with a Weston normal element having a temperature of 25°. Then

$$E_N = 1.0184 \text{ volts (see p. 302).}$$

A resistance of 5141.8 ohms ( $= AS_1$ ) is introduced into the resistance-box I.

A resistance of 4858.2 ohms ( $= S_1B$ ) is introduced into the resistance-box II.

The galvanometer then indicates no current, wherefore

$$E_A = \frac{10000}{5141.8} E_N = \frac{10000}{5141.8} 1.0184 \text{ volts,}$$

and (see the above)

$$E_{\text{Daniell}} = \frac{5452.8}{5141.8} 1.0184 \text{ volts} = 1.0799 \text{ volts.}$$

In many instances it may also be of physiological\* importance to determine the difference of potential between a metallic electrode and the solution of an electrolyte. Thus it might be of importance to know the difference of potential that exists (at a known temperature) between copper and a copper sulphate solution of a known concentration.

To determine this difference the system copper-copper sulphate solution is connected with a so-called *normal electrode* † illustrated in Fig. 48.

The latter consists of a glass tube, two centimetres wide,

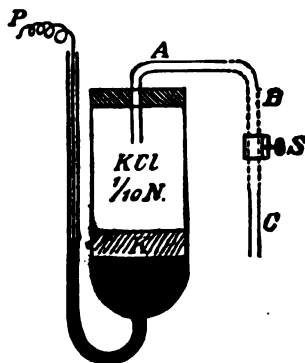


FIG. 48.

to which has been fused a glass capillary. Chemically pure mercury is introduced into the wide tube (see p. 311). A platinum wire, *p*, passes through the capillary into the mercury. ‡

\* See, for example, Oker-Blom, *Pflügers Arch.* **84**, 191 (1901).

† Ostwald, *Lehrbuch der allgemeinen Chemie* (2. Aufl.) II, 947 (1893); Coggeshall, *Zeitschr. f. physik. Chem.* **17**, 62 (1895); Richards, *ibid.* **24**, 39 (1897); Willmore, *ibid.* **35**, 291 (1900); Ostwald, *ibid.* **35**, 333 (1900).

‡ For other forms of the normal electrode see R. Lorenz, *Elektrochemisches Praktikum*, Göttingen 1901, p. 163.

Upon the mercury is placed a layer (*K*) of finely powdered calomel ( $\text{HgCl}$ ), and upon this a normal solution of potassium chloride (74.6 grams  $\text{KCl}$  per litre).\* The wide tube is closed with a rubber stopper perforated by a glass tube. This tube dips into and is filled with the potassium chloride solution. It is connected with a rubber tube *B* which can be closed by the screw pinch-cock *S*.

The electromotive force of a normal electrode is  $-0.560$  volt; the mercury forms the positive, the potassium chloride the negative pole. The glass tube *C* after being filled with the potassium chloride solution is dipped into the copper sulphate solution. In this way a galvanic element is formed according to the following plan:



the electromotive force of which can be determined in the ordinary way by Poggendorff's method.

The difference of potential between the copper and the copper sulphate solution can now be calculated by observing the following rules:†

1. By the anode is always meant that pole by which the positive electricity enters the galvanic cell.
2. The direction of the flow of the electricity is determined by measuring the combination: normal electrode | electrode under examination.
3. The formula for the measurement is written in such a way that the anode comes first.
4. The difference in potential between the copper and the copper sulphate solution is then calculated from the equation

$$+ E = e_a - e_b,$$

\* Since the normal electrode is subject to certain variations, the so-called *decinormal electrode* has come into use more recently. In this, instead of a  $\frac{1}{10}$ N. potassium chloride solution, a  $\frac{1}{100}$ N. solution of the salt is used. The electromotive force of this electrode is  $-0.616$  volt.

† See Lorenz, l. c. 167

wherein  $E$  is the measured electromotive force of the entire system,  $e_a$  the potential of the anode, and  $e_k$  the potential of the cathode.

In this calculation we make the unknown potential (according to circumstances either  $e_a$  or  $e_k$ ) equal to  $X$ , and the normal electrode, always with its negative sign, is introduced into the above algebraic equation. For example, in the combination, copper, copper sulphate  $\frac{1}{2}$  N., normal electrode, the current flows (within the element) from mercury to copper. The element has an electromotive force of 0.025 volt.

Since Hg is the anode, we write

$$\underbrace{\text{Hg} \cdot \text{HgCl} \mid \text{KCl}}_{e_a} - \underbrace{\text{CuSO}_4 \mid \text{Cu}}_{e_k} = 0.025,$$

and obtain the equation

$$-0.560 - X = 0.025,$$

wherefore

$$X = -0.595 \text{ volt.}$$

## SEVENTEENTH LECTURE.

### Electromotive Force (Continued).

#### THE THEORY OF GALVANIC ELEMENTS.

As has already been pointed out, Nernst (1889) has worked out a theory of galvanic elements based upon the theories of osmotic pressure and electrolytic dissociation which explains the phenomena observed therein not only qualitatively but also quantitatively. It explains how the electromotive force of the so-called *reversible cells* comes to pass, and consequently solves a problem that has occupied physicists and chemists since the time of Volta.

To illustrate the idea of a *reversible cell* let us imagine a Daniell element the circuit of which is closed by a wire; into this circuit is introduced another element in such a way that the similar poles of the two elements are connected with each other. If now the electromotive force of the Daniell element is greater than that of the second element, the Daniell cell will send its current through the new element. When 96538 coulombs have flowed through the element, one gram-equivalent of copper will have been precipitated upon the copper plate in the Daniell cell, while one gram-equivalent of zinc will have gone into solution; for we know that 96538 coulombs can migrate only with a simultaneous movement of one gram-equivalent of any element (in this case the copper of the copper solution or the zinc of the zinc sulphate solution). If we substitute for the second

cell one that has a greater electromotive force than the Daniell cell, the current will flow in the opposite direction through the Daniell element.

When 96538 coulombs have again flowed through the cell, one gram-equivalent of copper from the copper plate will have gone into solution, and one gram-equivalent of zinc will have been precipitated from the zinc sulphate solution upon the zinc plate.

After this the Daniell element is again in the same state as originally. The electromotive force of the element has undergone no change, since both the electrodes and the electrolytes in which these are immersed have remained entirely unchanged.

The Daniell cell is called a *reversible* element; the characteristic feature of such a cell is this, that its electromotive force does not change when a current is sent through it in a direction opposite to that furnished by the element itself.

In order to learn how to calculate the electromotive force of such a system, we will follow Nernst\* in the development of his idea of *electrolytic solution tension*, or as it has been called by Ostwald, *electrolytic solution pressure*.

If water is put into a closed space it vaporises, that is, molecules of water vapour are formed which collect in the space above the liquid; at a definite temperature equilibrium is established between the water and the water vapour as soon as the latter has reached a definite pressure (*vapour tension* at the given temperature).

Now Nernst points out that if we assume with van't Hoff that the molecules of a substance dissolved in a solvent exist under a definite pressure (the osmotic pressure of the

\* Zeitschr. f. physik. Chem. 4, 129 (1889).

dissolved substance), we must ascribe to every substance in contact with a solvent a certain tension, with which it endeavours to go into solution. If, for example, we put sugar (or salt) into pure water, the sugar (or salt) molecules are driven into this solvent; the pure water acts like a vacuum toward the sugar (or salt) molecules.

The tension with which the molecules endeavour to go into solution is called the *solution tension* (solution pressure) of the given substance.

The molecules can no longer go into solution, in other words, equilibrium will be established between the solution and the solid substance lying upon the bottom of the vessel as soon as the osmotic pressure of the dissolved molecules is equal to the solution tension that drives them into solution.

Now these considerations have been extended by Nernst to the case in which we deal with the transition of substances into the ionic state.

The metals, likewise hydrogen, can furnish only positive ions; chlorine, bromine, iodine, etc., only negative ions.

If a metal is dipped into a solution of one of its salts (for example, zinc into a zinc sulphate solution), it sends its ions into the solution with a certain solution tension (*the electrolytic solution tension*). This pressure opposes the osmotic pressure of the metallic ions that are already present in the solution. If the electrolytic solution tension of the metal is  $P$ , the osmotic pressure of the metallic ions in the solution  $p$ , then, when  $P > p$ , a number of positive metallic ions will go into solution in the first differential of time; the solution will in consequence assume a positive charge; at the same time the metal will assume a negative



charge. The negative electricity at the surface of the metal will attract the positive ions of the solution, and in consequence at the area of contact between the metal and the solution a so-called *electrical double layer* will be formed. Now since the metal is negatively charged while the solution is positively charged, a double layer will tend to drive the metallic ions out of the solution to the metal, where they give up their electrical charges and go over into the neutral metallic state; the double layer therefore opposes the solution tension of the metal. Equilibrium will be established between these two opposing forces as soon as both are of the same magnitude. The action of these two forces brings about a difference in potential (electromotive force) between the metal and the solution.

If  $P > p$ , that is, if the solution is positive as compared with the metal, the resulting electromotive force causes an electrical current that moves from the metal to the solution.

If  $P < p$ , the metallic ions in the solution move toward the metal and are there precipitated, and the metal assumes a positive charge as compared with the solution. The positive charge of the metal attracts the negative ions of the solution, and in consequence another electrical double layer is formed, this time, however, in a way opposite to that just described. The metallic ions are precipitated from the solution, until the repulsion of these ions by the positively charged metal is equal to the osmotic pressure that makes them go out of solution. The result of this action is the production of a difference in potential between the metal and the solution. The current produced in this case flows from the solution to the metal.

Finally, if  $P = p$ , that is, if equilibrium exists even in the

first differential of time, when the metal comes in contact with the solution no difference in potential arises between the two.

Every metal has, at a definite temperature, a definite electrolytic solution tension:

If the electrolytic solution tension of different metals is investigated (we cannot here discuss the method by which this can be done), it is found that aluminium, iron, nickel, magnesium, zinc, and cadmium are always negative when brought in contact with solutions of their salts; this means that their electrolytic solution tension is greater than the osmotic pressure of the metallic ions in any solution that can be prepared from their salts. This is attributable to the fact that the solubility of these salts is never so great that the osmotic pressure of the metallic ions in the given solutions equals the very high electrolytic solution tension of the metal.

Mercury, copper, gold, and silver are charged positively when immersed in solutions of their salts, since the electrolytic solution tension of these metals is so low that it is usually less than the osmotic pressure of the metallic ions in solution.

Only in exceedingly dilute solutions would it be possible for the osmotic pressure of the metallic ions to be lower than the electrolytic solution tension of these metals, and under these conditions the metal would become negative in the solution.\*

\* We cannot here discuss how the magnitude of electrolytic solution tension is determined. Calculation shows that this pressure is exceedingly high, at room temperature, for such metals as zinc, cadmium, etc., while for gold, silver, etc., it is exceedingly low. According to Neumann, for example, [*Zeitschr. f. physik. Chem.* 14, 193 (1894),] the electrolytic solution tension of zinc in normal solu-

Nernst has shown upon thermodynamical grounds that when a metal is dipped into the dilute solution of one of its salts the difference in potential between this electrode and the solution may be represented by the following equation:

$$E = \frac{0.0002}{n} T \log \frac{P}{p} \text{ volt.} \quad (1)$$

Herein  $E$  is the difference in potential in volts, and  $n$  the valency of the metal of the electrode,—equal to 2, therefore, for a copper electrode, 1 for a lithium electrode.  $T$  is the absolute temperature of the electrode (or the solution),  $P$  the electrolytic solution tension of the metal used for the electrode, and  $p$  the osmotic pressure of the metallic ions in the solution.

If, therefore, the valency ( $n$ ), the electrolytic solution tension ( $P$ ) of the copper, and the osmotic pressure ( $p$ ) of the copper ions in a dilute copper sulphate solution at the absolute temperature ( $T$ ) are known, the difference of potential between the electrode and the solution can be calculated in volts.

In the case of the Daniell element upon a closed circuit, for example, which is built upon the plan

copper—dilute copper sulphate solution—dilute zinc sulphate  
solution—zinc,

the electromotive force is seen to be composed of the following differences in potential:

- a. Difference in potential between copper and zinc;
- b. Difference in potential between copper and copper sulphate solution;

tion is  $9.9 \times 10^{18}$  atmospheres, for silver  $2.3 \times 10^{17}$  atmospheres. This means that when a zinc rod is, at room temperature, dipped into a zinc sulphate solution containing 80.7 g.  $\text{ZnSO}_4$ , the zinc ions are driven into the solution with a pressure of  $9.9 \times 10^{18}$  atmospheres.

e. Difference in potential between copper sulphate solution and zinc sulphate solution;

d. Difference in potential between zinc sulphate solution and zinc.

Now the differences in potential under *a* and *c* are very low compared to those given under *b* and *d*, and so may be neglected.

According to equation (1) the difference in potential between the copper and the copper sulphate solution ( $E_c$ ) amounts to

$$E_c = \frac{0.0002}{n_c} T \log \frac{P_c}{p_c},$$

wherein  $n_c$  is the valency of the copper ( $n_c = 2$ ),  $P_c$  its electrolytic solution tension at the absolute temperature  $T$ ,  $p_c$  the osmotic pressure of the copper ions in the copper sulphate solution at this temperature, and  $T$  the absolute temperature of the Daniell element.

In the same way the following equation holds for the difference in potential between the zinc electrode and the zinc sulphate solution ( $E_z$ ):

$$E_z = \frac{0.0002}{n_z} T \log \frac{P_z}{p_z}.$$

The electromotive force of the Daniell element ( $E$ ) is therefore

$$E = E_z - E_c = \frac{0.0002}{n_z} T \log \frac{P_z}{p_z} - \frac{0.0002}{n_c} T \log \frac{P_c}{p_c},$$

or, since  $n_z = n_c = 2$ ,

$$E = 0.0001T \left( \log \frac{P_z}{p_z} - \log \frac{P_c}{p_c} \right).$$

The practical application of equation (1) becomes simpler when we deal with a so-called *concentration cell*. Such a chain is formed when two beakers are filled with differently concentrated (dilute) solutions of any metallic salt, such as silver nitrate, and silver plates are dipped into them, while a siphon with equal arms and filled with silver nitrate solution connects the two dilute solutions.

If the two silver plates are connected by a silver wire, a current flows through it. What happens in the element is the following: The silver endeavours to go into solution in consequence of its electrolytic solution tension. In the more

dilute silver nitrate solution the osmotic pressure of the silver ions is lower than that in the more concentrated solution. The osmotic pressure of the more dilute solution is consequently less opposed to the solution tension of the silver electrode immersed in it than that of the more concentrated solution. In the dilute solution the electrode sends its positive ions into solution and assumes a negative charge, while in the more concentrated solution silver ions are deposited upon the silver electrode. The concentration of the dilute solution in consequence increases, while that of the concentrated solution decreases, and this goes on until both solutions have the same concentration.

Within the chain the current moves from the dilute to the concentrated solution, while in the external circuit it moves in the opposite direction.

The electromotive force of such a chain is made up of three components:

a. The difference in potential ( $E_1$ ) between the first silver electrode and the dilute solution;

b. The difference in potential ( $E_2$ ) between the second silver electrode and the concentrated solution;

c. The difference in potential ( $E_3$ ) between the two solutions.

If we make use of equation (1) to determine the differences in potential  $E_1$  and  $E_2$ , then

$$E_1 = \frac{0.0002}{n_s} T \log \frac{P_s}{p_d} \text{ volt,}$$

$$\text{and} \quad E_2 = \frac{0.0002}{n_s} T \log \frac{P_s}{p_c} \text{ volt,}$$

wherein  $n_s$  is the valency of the silver ( $= 1$ ),  $P_s$  the electrolytic solution tension of this metal at the absolute temperature  $T$  of the chain,  $p_c$  the osmotic pressure of the silver ions in the concentrated solution,  $p_d$  that in the dilute solution.

The value of  $E_3$ , which can be calculated by a method given by Nernst and Planck, but into which we cannot enter here, is small when compared with  $E_1$  and  $E_2$ , and will be left out of consideration here.

The electromotive force of the cell is therefore

$$E = E_1 - E_2 = \frac{0.0002}{n_s} T \left( \log \frac{P_s}{p_d} - \log \frac{P_s}{p_c} \right) \text{ volt,}$$

or 
$$E = \frac{0.0002}{n_s} T \log \frac{p_c}{p_d} \text{ volt.} \quad (2)$$

The electromotive force is therefore solely dependent upon the relation that the osmotic pressures ( $p_c$  and  $p_d$ ) of the metallic ions in the two solutions bear to each other and the valency ( $n_s$ ) of the metals, and is independent of the negative ions in the solution and the nature of the metal used for the electrodes.

It must further be noted that in case the solutions are very dilute, their concentrations (number of mols per litre) can be substituted for the relation of the osmotic pressures  $\left(\frac{p_c}{p_d}\right)$  to each other.

If, for example, the more dilute of the two solutions is  $\frac{1}{1000}$  normal, the more concentrated  $\frac{1}{100}$  normal, we substitute for the relation  $\frac{p_c}{p_d} \frac{1}{100} = 10$ ; wherefore  $\log \frac{p_c}{p_d} = \log 10 = 1$ .

If the solutions are not so dilute that the dissolved substance may be considered as completely dissociated, then the number of metallic ions present per litre can be determined by measuring the degree of dissociation.

Thus, Nernst found the electromotive force of a concentration cell built upon the plan:

Silver— $\frac{1}{100}$ N. AgNO<sub>3</sub> solution— $\frac{1}{1000}$ N. AgNO<sub>3</sub> solution—silver  
to be 0.055 volt at 18° ( $T = 291$ ), ( $n = 1$ ), while calculation by equation (2) gives

$$E_1 = 0.0002 \times 291 \times \log 8.71 = 0.0547 \text{ volt,}$$

when it is borne in mind that the measurement of the conductivity of these solutions shows that the concentrations of the silver ions are to each other not as 100 : 1000 (= 1 : 10), but as 1 : 8.71.

The agreement between the value calculated (0.0547 volt) and that found experimentally is very satisfactory.

In the concentration cell just described the electrodes were made of metal. Elements can, however, be constructed in which gases serve as electrodes. So-called *gas cells* are then formed, the study of which has been of great im-

portance in electro-chemistry. We shall discuss them here in so far as they have become of physiological importance.

Let us imagine a hydrogen electrode (how such electrodes are made for practical purposes will be described immediately) immersed in an electrolyte containing hydrogen ions, and a second entirely similar electrode immersed in an electrolyte in which hydrogen ions are also present, but in a lower concentration than in the first solution. If both solutions are connected with each other by a siphon having equal arms and filled with the electrolyte, we have a concentration chain that is entirely similar to the silver nitrate chain described above. If we choose two acid solutions of different concentrations as the electrolytes containing hydrogen ions, and close the circuit, then the gaseous hydrogen of the electrode in the dilute solution will, in consequence of its solution tension, go into solution, since the osmotic pressure of the hydrogen ions in this solution opposes the electrolytic solution tension of the electrode to a less degree than the osmotic pressure of the hydrogen ions in the concentrated solution. In the latter a corresponding amount of hydrogen ions will move from the solution to the electrode and there give up their electrical charge; that is, they will go over into the electrically neutral (gaseous) state.

The more dilute solution will therefore become more concentrated with respect to hydrogen ions, while in the more concentrated solution the reverse process will occur. As soon as both solutions have attained the same hydrogen ion concentration, the flow of electricity in the chain will cease.

Hydrogen electrodes can be made by covering two platinumised (see p. 202) sheets of platinum with hydrogen.\* As

\* See Böttger, *Zeitschr. f. physik. Chem.* **24**, 253 (1897).

is known to you, platinum-black, with which the plates become covered, has the property of holding—of *absorbing*—large amounts of hydrogen. Such an electrode conducts itself in its electromotive behaviour as a plate of hydrogen.

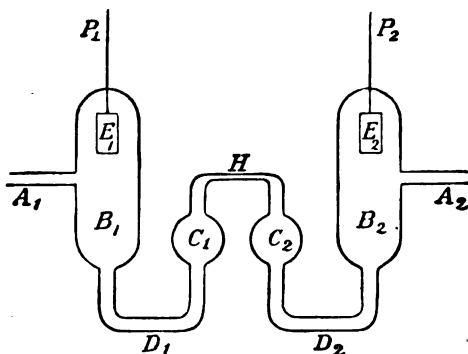


FIG. 49.

Fig. 49 represents a hydrogen chain.

$A_1B_1D_1C_1$  and  $A_2B_2D_2C_2$  are glass vessels that can be connected with each other by the small-calibred glass tube  $H$ .  $E_1$  and  $E_2$  are platinised sheets of platinum connected with the wires  $P_1$  and  $P_2$  which are fused into the glass.

$A_1B_1D_1C_1$  and  $A_2B_2D_2C_2$  are filled with acid solutions of different concentrations, while hydrogen is passed into the vessels through  $A_1$  and  $A_2$ . After the electrodes have become covered with hydrogen,  $H$  is also filled with one of the acid solutions, and  $C_1$  and  $C_2$  are connected with each other.  $A_1$  and  $A_2$  are then closed.

We cannot here enter into a discussion of the accurate calculation of the electromotive force of such a chain. This can be done by utilising the formula of Nernst and Planck,





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